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# Notch Coordinates Periodontal Ligament Maturation through Regulating Lamin A

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# Journal of Dental Research

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Keywords:	Tooth development, Periodontal ligament (PDL), Occlusion, Molecular biology, Cell biology
Abstract:	<p>Tooth eruption is a continuous biological process with dynamic changes at cellular and tissue levels particularly within the periodontal ligament (PDL). Occlusion completion is a significant physiological landmark of dentition establishment. However the importance of the involvement of molecular networks engaging in occlusion establishment on the final PDL maturation are still largely unknown. In this study, using rat and mouse molar teeth and a human PDL cell line for RNAseq and proteomic analysis, we systematically screened the key molecular links in regulating PDL maturation before and after occlusion establishment. We discovered Notch, a key molecular pathway in regulating stem cell fate and differentiation, is a major player in the event. Intercepting Notch pathway by deleting its key canonical transcriptional factor: RBP-Jkappa using conditional knock out strategy in the mice delayed PDL maturation. We also identified that Lamin A, a cell nuclear lamina member, is one unique marker of PDL maturation and its expression is under the control of Notch signalling. Our study therefore provides a deep insight of how PDL maturation is regulated at molecular level and we expect the outcomes to be applied for a better understanding of the molecular regulation networks in physiological conditions such as tooth eruption and movement, and also for periodontal diseases.</p>

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## **Notch coordinates periodontal ligament maturation through regulating Lamin A**

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**Running title:** Notch controls periodontal ligament development

**Key words:** Tooth; Periodontal ligament; Occlusion; Notch, Lamin A

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For Peer Review

## Abstract

Tooth eruption is a continuous biological process with dynamic changes at cellular and tissue levels particularly within the periodontal ligament (PDL). Occlusion completion is a significant physiological landmark of dentition establishment. However the importance of the involvement of molecular networks engaging in occlusion establishment on the final PDL maturation are still largely unknown. In this study, using rat and mouse molar teeth and a human PDL cell line for RNAseq and proteomic analysis, we systematically screened the key molecular links in regulating PDL maturation before and after occlusion establishment. We discovered *Notch*, a key molecular pathway in regulating stem cell fate and differentiation, is a major player in the event. Intercepting *Notch* pathway by deleting its key canonical transcriptional factor: *RBP-Jkappa* using conditional knock out strategy in the mice delayed PDL maturation. We also identified that *Lamin A*, a cell nuclear lamina member, is one unique marker of PDL maturation and its expression is under the control of *Notch* signalling. Our study therefore provides a deep insight of how PDL maturation is regulated at molecular level and we expect the outcomes to be applied for a better understanding of the molecular regulation networks in physiological conditions such as tooth eruption and movement, and also for periodontal diseases.

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**Introduction**

Tooth eruption is accompanied by the development and maturation of PDL (Cho and Garant 2000). Recent studies suggest PDL originates from dental follicle progenitors that can be either *Osx Cre* (Ono et al. 2016) and/or *PTHrP-Cre* positive (Takahashi et al. 2019). During pre-occlusal eruption phase, a tooth performs axial movement till occlusion is reached, as such no exogenous tension or compression forces are applied on PDL yet. In parallel to the tooth eruption, mesenchymal cells inside PDL secrete increasing amounts of extracellular matrix such as collagen and elastin, which further polymerise into collagen fibres and elastic fibres (Berkovitz and Moxham 1990). Upon contacting the opposite tooth, i.e. the occlusion is established and root development is completed. The PDL fibres are then organized into thick bundles and suspend the tooth in the alveolar socket, hence are under the challenge of constant stretching force, facilitating the tooth to adapt to the biting force and prevent tissue damages (Beertsen et al. 1997).

The molecular networks and mechanisms linking occlusion establishment with PDL development has not been previously systemically screened yet. In many systems, *Notch* signalling plays a key role in controlling stem cell maintenance and differentiation (Cheung and Rando 2013). Notch proteins are transmembrane receptors that act through cell-to-cell and cell-to-matrix signalling (Giaimo and Borggreffe 2018). Binding of Notch receptor to ligand leads to the cleavage of the receptor’s intramembrane sites and releasing of the intracellular domain (ICD), which translocates into nucleus and binds to the RBP-Jkappa transcription effector complex. Notch receptors are also sensitive to extracellular forces, and a small amount of force can reveal the S2 cleavage site for proteinases, which leads to release of the ICD domain and gene transcription (Kopan and Ilagan 2009). In the tooth, increasing evidence suggests that *Notch* is essential in the pulp and cervical loop stem cell maintenance and terminal odontoblast differentiation, as well as in tooth pulp wound healing ((Kurpinski et al. 2010;

Lovschall et al. 2007), and Walker et al., in press). However, although *Notch* pathway has been implicated in inducing osteogenic differentiation of cultured PDL cells (Li et al. 2014; Nakao et al. 2009; Osathanon et al. 2013), its function in periodontal ligament development and particularly maturation has not been elucidated.

In this study, we provide novel *in vivo* and *in vitro* evidence highlighting the important role of *Notch* pathway in periodontal ligament development and maturation with nuclear lamina protein *Lamin A* as a direct target.

## Materials & Methods

### Animals

The Wistar rat and tooth eruption stages were determined based on data of a previous study (Denes et al. 2018) and verified by micro-CT scans. The work was approved by the ethics committee of animal research of the Canton of Geneva (n° GE/72/15). *RBP-Jkappa<sup>loxp/loxp</sup>* and *Coll α2-Cre* mice are as reported previously (Hu et al. 2010).

### Laser capture microdissection

Mandibles were dissected and immediately frozen in PrestoChill (Milestone, Type 51420) at -40°C and stored at -80°C. Sections were performed with a cryostat and transferred to PET-membrane slides with the CryoJane Tape system (Leica Biosystems). Slides were dehydrated successively with 70%, 95%, 100% EtOH at -20°C. Microdissection of the periodontal ligament (PDL) was performed at the cervical 1/3 PDL region. For each developmental stage, 4 individual animals were used.

### RNAseq statistical analysis

RNA extraction was performed according to RNeasy Micro Kit (Qiagen®). RNA quantity and quality was evaluated with Agilent 2100 Bioanalyzer (Agilent Technologies). RIN number



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3 equal or greater to 7 was required for the sample for analysis. Total RNA was amplified and  
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5 Next-Generation Sequencing with the Illumina HiSeq 4000 was performed with protocol  
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7 Smarter + Nextera and the reference genome Rattus Norvegicus. Quality was assessed by  
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9 FastQC v.0.11.5 and resulted in values between 32 and 40 (error: 1/1'000 to 1/10'000). The  
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11 reads (length=100 bp) were mapped with the STAR v2.5.3a software to the reference genome  
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13 and showed good alignment percentage (71.7%  $\pm$ 5.9). Biological quality control and  
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15 summarization were done with the PicardTools v2.9.0 with percentage of mRNA bases as  
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17 average 63%. The normalization and differential expression analysis was performed with the  
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19 R/Bioconductor package edgeR v.3.16.5 and statistical significance was assessed with General  
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21 Linear Model, negative binomial distribution and a quasi-likelihood *F*-test. Threshold for  
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23 significance was set at p-value <5% and fold change (FC)>1.5. The RNAseq data can accessed  
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25 through number: GSE129458 from <https://www.ncbi.nlm.nih.gov/geo/>. Enrichment analysis  
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27 of RNAseq was performed with GO Ontology database and analyzed with PANTHER  
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29 Overrepresentation Test. Fischer test was used with false discovery rate (FDR) correction  
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31 applied. Biological processes, molecular functions and cell compartment analyses were  
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33 classified based number of genes.  
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43 **Rat paraffin sections**

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45 The cryoembedded mandibles were washed in distilled water to remove MCC, fixed in 4%  
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47 paraformaldehyde (Merck), decalcified in Osteosoft (Sigma-Aldrich) or 14% EDTA (pH7.4)  
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49 for a period of 6-weeks, embedded in paraffin. The paraffin blocks were cut into sections of  
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51 3 $\mu$ m thickness at the second root-pair of the first molar for rat samples and 10 $\mu$ m for mouse  
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53 teeth.  
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60 **Immunohistochemistry/Immunofluorescence**

4-5 individual animals were used for each genotype at each defined stage. Osteosoft (Sigma-Aldrich) or 14% EDTA (pH7.4) decalcified samples were cut into 3 $\mu$ m thickness sections. The sections were deparafinized and antigen retrieval was done in citrate buffer (pH8.0) at 98°C for 20 min or a microwave at 750w for 1 minute, followed by blocking in PBS containing 5% donkey serum, 0.25% cold water fish gelatine and 0.25% bovine serum albumin for 1h at room temperature and incubated with primary antibodies for overnight at 4°C, and secondary antibodies for 2h at room temperature. and counterstained with 4'-6-diamidino-2-phenylindole (DAPI). Imaging was performed with a Leica DMI6000 confocal microscope. For immunohistochemistry, Vectastain with DAB substrate were used. For details please see Appendix Table 3. Goldner staining was used for collagen staining.

### Cell cultures and treatment

Human periodontal ligament fibroblasts (hPLF, ScienCell, Catalog #2630) were cultured in DMEM/F-12 with 20% FBS and 1% Antibiotic-Antimycotic. For Jagged1 treatment, after overnight seeding and cell confluency reached to 70%, Jagged1 was added to the medium to reach to a final concentration of 100ng/ml. Cultures were fixed after 24h of Jag1 treatment with 4% PFA at room temperature for 20 minutes and then washed 2x with PBS (10mM).

Stretching experiments were performed with the stretching device and silicone membranes (Strex USA, ST-140-04) (Appendix Figure 1 and 2). The membranes were coated with rat tail collagen type I (Life Technologies, A1048301) and HCl at 1:1 ratio overnight at 37°C. Cells were seeded as 2x10<sup>5</sup> cells per membrane. Cells were stretched for 6h, 12h and 24h at 37°C alongside controls.

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**Quantitative real-time RT-PCR**

Tirpilated samples were used for each gene analysis. Total RNAs was extracted using the penol-chloroform technique and reverse transcription of was achieved with High-Capacity cDNA synthesis kit (Thermo Fisher Scientific), as previously described (Singer et al. 2019). The PCR reaction was performed with SYBR Green I Master Mix (Roche) on a LightCycler 480 II Real-Time PCR system (Roche Molecular Diagnostics) for 45 cycles. *36 beta4* gene was used as housekeeping gene to normalize samples with the  $2^{-\Delta\Delta C_t}$  method. All analyses were performed with three replicates as described previously (Hu et al. 2012). For the primers used in this study please see Appendix Table 3.

**Nanoscale Liquid Chromatographic–Electrospray Ionization–Tandem Mass Spectrometry (nLC–ESI–MS/MS)**

Duplicted samples were used for the analysis. In-gel tryptic digestion of proteins was carried out as described in (Costa et al. 2018). Peptides were separated on an HSS T3 column (waters) and injected into an Orbitrap Elite MS using a 90 min gradient from 2 to 30% acetonitrile, 0.1% formic acid. Full MS scans in the orbitrap and fragmentation of 20 most intense precursors in parallel was done. Protein identification and label-free quantification was done with MaxQuant (Cox et al. 2014) and further statistical analysis with Perseus (Tyanova et al. 2016). Differential expression of fold change > 2 was analyzed with Gene Ontology (GO) enrichment of biological processes powered by Panther Database (pantherdb.org) and clustering was performed with String Database v11.0 (string-db.org). For *in vivo* proteomic analysis, electrospray ionization Liquid-Chromatography-Mass Spectrometry/Mass Spectrometry (ESI-LC-MSMS) was performed on rat mandible periodontal ligament, dissected with laser capture microdissection

technique. The results can be access with number: PXD013379 from <https://www.ebi.ac.uk/pride/archive/>.

## Western Blotting

Cells were washed with HBSS, collected at 10,000 rpm for 10 minutes at 4°C. The pellet was re-suspended in ice-cold radioimmunoprecipitation assay buffer (89901, Pierce) with protease & phosphatase inhibitor cocktail (78442, Pierce) and incubated on ice for 30 minutes then spun down at 10,000rpm for 10 minutes at 4°C. The supernatant was collected and quantified with BCA method (23225, Pierce). Protein were separated with 4-12% NuPAGE Novex Bis-Tris gel and transferred to polyvinylidene membrane, detected with iBind Flex Western device (SLF2000S, Invitrogen). Antibodies were diluted in iBindFlex solution (SLF2020, Invitrogen). Membranes were scanned with C-DiGit scanner (Li-COR, 3600-00). For antibodies see Appendix Table 3.

## Results

### PDL has distinct gene expression profile changes upon occlusion establishment

We selected postnatal day 18 (P18, pre-occlusion eruption) and 28 (P28, 1 week after occlusion establishment) of the Wistar rat's second root pair of the first lower molar as the studying models. The eruption stage was confirmed by daily *in vivo* micro-CT imaging based on our previous study (Denes et al. 2018). Histological analysis and micro-CT confirmed that the root development of P18 tooth was at the initial elongation stage, while at P28 the root development reached near completion (Figure 1A and Appendix Figure 1A). Trichrome staining showed P28 PDL was abundant with collagen fibres, comparing to P18 (Figure 1B). As well, P28 PDL expressed significantly higher level of Periostin (Figure 1C). To explore the transcriptome changes of PDL, we next performed RNAseq analysis on the PDL at indicated

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3 stages (RNAseq accession number: GSE129458). Among a total of 12,742 detected genes, we  
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5 identified 1,090 genes were upregulated and 1,035 were downregulated with more than 1.5  
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7 fold changes with p value < 5%, at P28 comparing to P18 (Appendix Table 1). Gene enrichment  
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9 analysis suggested P28 has significantly increased cellular process and protein binding events  
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11 comparing to P18 (Figure 1D). Heatmap of genes identified by Metacore pathway map analysis  
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13 shows consistent expression throughout samples (Figure 1E). Using GO analysis to examine  
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15 the biological processes and Metacore process networks, as expected, we have identified that  
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17 “biomineral tissue development” and “muscle contraction” are among the most significantly  
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19 changed biological processes (Figure 1F and Appendix Figure 1B).

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26 **Notch signalling is dynamically changed before and after occlusion is established**

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28 String analysis suggested *Notch* pathway acted as a center of the molecular networks (Figure  
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30 2A). Metacore pathway map analysis further confirmed *PI3K* and *Notch* signalings are the top  
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32 two pathways affected (Figure 2B). As the function of *Notch* signaling has not been described  
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34 previously in PDL *in vivo*, particularly in the occlusion establishing stage, we therefore  
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36 continued focusing on that pathway for our study.

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40 In the RNAseq analysis, *Notch1*, *Notch4* and *Dll1* are the *Notch* pathway members that  
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42 were significantly upregulated in the P28 PDL comparing to P18 (p<0.05), and *Jagged 1* was  
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44 upregulated with a marginal p value (p = 0.067), and *Furin* was significantly downregulated  
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46 (p<0.05) (Figure 2C). We next compared Notch protein expression with immunofluorescence  
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48 analysis. Consistent with the RNAseq results, we found that both total Notch1 and its ICD were  
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50 increasingly expressed in the P28 PDL (Figure 2D and E) as well as Notch ligands such as Dll1  
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52 (Figure 2F), in parallel to the increased PDL maturation marker: Osteopontin (Figure 2G) (Rios  
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54 et al. 2008). Interestingly, when we evaluated in parallel the other Notch receptor, Notch2  
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56 ICD’s expression was at its highest level at pre-occlusal eruption stage and decreased thereafter  
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(Figure 2H), suggesting that Notch1 and Notch2 receptors play significant however different roles in PDL development.

### **Intercepting Notch pathway delays PDL development and tooth eruption**

To confirm the function of *Notch* pathway in PDL development during occlusion establishment, we adopted the mesenchymal conditional *RBP-Jkappa* knockout transgenic mouse model, where the *Cre* recombinase expression is under the control of *Collagen 1  $\alpha$ 2* promoter (Hu et al. 2010). Staining with specific antibodies, we observed abundant Cre protein expression in the PDL cells confirmed the deletion of the *RBP-Jkappa* gene in PDL cells, as well as osteoblasts at the bone surface (Figure 3A). By crossing the *Collagen 1  $\alpha$ 2 Cre* transgenics with *RBP-Jkappa<sup>flox/flox</sup>* mice (Hu et al. 2012; Hu et al. 2010), phenotypically at P21 when the tooth eruption is complete in the WT mice, the mice with *RBP-Jkappa* deletion in PDL cells encountered significant delay of tooth eruption and root development (Figure 3B). Macroscopy analysis revealed the *RBP-Jkappa* knockout mice had smaller mandibles (Figure 3C) and molar crown size. (Figure 3D). Stereomicroscopy and microCT analysis and quantification (Figure 3G) suggested that while initially the root development is delayed in the *RBP-Jkappa* knockout mice (Figure 3E and G), the tooth crown eruption in the mutants could still be eventually completed (Figure 3F) and root length had no difference comparing the control with the knockout mice (Figure 3G). Consistently, immunofluorescence analysis on Periostin expression suggested at P4 there were no expression of the marker (Appendix Figure 2A), while at P10 and P14 the knockout mice has a significantly delayed expression (Figure H&I). However, after two months there are no notable difference between the control and knockout animals' PDL (Figure 2J).

### ***In vitro* stretching mirrored occlusion establishment effects on PDL cells**

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To confirm if the key molecular changes identified in the *in vivo* RNAseq analysis were due to the stretching of PDL mesenchymal cells and its relevance to human, we next cultured human PDL cells and mimicked occlusive stretching force by inducing reciprocal force on the cells on an automatic cell stretching system (Appendix Figure 2B and C). Real-Time RT-PCR results confirmed significant induction of the mRNA expression of *Notch* pathway members such as *Jagged 1*, *Dll1* and *Hey1* (Figure 4A), as well a panel PDL cell differentiation markers including Osteopontin (Figure 4B). To further gain insight of the molecular targets of the PDL in responding to stretching force, we performed proteomic analysis on the stretched PDL cells and found extracellular matrix protein such as collagen and periostin and the RhoA-CDC42 associated cytoskeleton regulating system were significantly changed (Figure 4C and D, and Appendix Table 2).

**Lamin A is a direct effector in PDL in responding to stretching and act as Notch downstream target**

By comparing the *in vitro* PDL cell stretching results with proteomic analysis from the *in vivo* PDL maturation (PRIDE number: PXD013379) and RNAseq analysis, we noticed the nuclear membrane protein: Lamin A was the only molecule displaying the same upregulation pattern across the three analyses (Figure 5A). Immunofluorescent analysis confirmed that Lamin A/C expression did increase in the P28 rat PDL, comparing with P18 samples (Figure 5B). Western Blot analysis suggested Lamin A protein level is specifically induced in the stretched human PDL cells but not Lamin C (Figure 5C). Similarly, treating PDL cells with Notch ligand: Jagged1 could induce Lamin A expression (Figure 5D). Finally, in the *RBP-Jkappa* knockout mice PDL, Lamin A/C expression was concomitantly reduced both at P10 and 2 months (Figure 5E and F). Therefore, *Lamin A* is indeed an indicator of PDL maturation that is under *Notch* signalling control and is positively regulated by stretching force.

## Discussion

The development of PDL, alveolar bone and cementum are closely linked events. So far, particularly for PDL and alveolar bone, it is still a dearth for finding genetic tools to dissect the specific populations inside the tissues, particularly for fibroblasts and osteoblasts. However, increasing evidence have already shown that multiple signalling pathways are closely involved in the periodontium development, such as *NFI-C* null mice abolish root development (Steele-Perkins et al. 2003) and conditional deletion of *Smad4* in tooth epithelium can impede root growth (Li et al. 2015), while conditional deletion PPR using PTHrP-Cre impede tooth eruption (Takahashi et al. 2019). *Notch* signalling is one of the key pathways in determining mesenchymal stem cell fate and cell differentiation such as in the muscles (Conboy et al. 2003; Conboy and Rando 2002). In bone and bone marrow mesenchymal progenitors, *Notch*'s function has been extensively descbed in protecting mesenchymal progenitors (Hilton et al. 2008). While in the tooth, previous reports and our findings suggest that *Notch* is important both for maintaining stem cells and differentiation but the functions are carried out via different Notch receptors: i.e. *Notch1* acts through maintaining stem cell pool and inducing cell differetnation and *Notch2* is rather responsible for maintaining transit amplying cells ((Mitsiadis et al. 2017; Zhang et al. 2008) and Walker et al. in press). In PDL, our results confirm that Notch1 is linked with PDL final development and completion, while interestingly Notch2 preferentially functions during the pre-occlusion stage. This might reflect a different role of *Notch2* in enhancing cell populating into the tissue, similar to the findings in the incisor mesenchymal stem cells (Walker et al. in press). Although we have not been able to achieve the mesenchymal specific conditional Notch receptor deletion models due to early death in embryonic stages (data not shown), it would be still interesting to apply inducible conditional deletion models to distinguish the different roles of Notch receptors in PDL development. As



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well, future studying Notch’s roles such as in PDL stem cell fate control, as well as aging are highly desired (Appendix Figure 3).

In addition, our results showed that blocking canonical *Notch* pathway by deleting *RBP-Jkappa* in the PDL delayed but did not inhibit tooth eruption and PDL maturation completely, suggesting that canonical *Notch* is dispensable in these events. Significantly, the Notch ligands: *Dll1*, *Dll4* and *Jagged1* expression are all highly elevated in the PDL cells upon stretching, suggesting the PDL cells play a central role in the tissue homeostasis, possibly through *Notch* pathway ligands production, to affect surrounding microenvironment, such as vascularisation through endothelial cell specific Notch4 receptor. One evidence to support this theory is that during orthodontic tooth movement, blood vessel proliferation and remodelling is among the early key events in the PDL (Rygh et al. 1986; Vandeyska-Radunovic et al. 1994).

Lamin A is an important nuclear envelope molecule for protecting cells from DNA damage and pre-aging and its mutation can cause laminopathies including Progeria (Broers et al. 2006; Eriksson et al. 2003; Worman 2012). Lamin A gene encodes two isoforms: Lamin A and C that are created from alternative splicing that encode important protein for nuclear envelopes. While Lamin C is shorter and produced directly, Lamin A, which is two exons longer at C-terminal, is required to pass prelamins A stage followed by a series of posttranslational modifications initiated from the farnesylation of C terminal cysteine (Lin and Worman 1993). We observed Lamin A transcription and translation were both elevated upon occlusion establishment, as well as under stretching condition in the PDL cells, which indicates its potential significant role in protecting the cells from stretching force induced cellular damages. The evidence that *Notch* signal activation by Jagged1 treatment could also elevate Lamin A but not Lamin C expression further confirmed that Lamin A potentially has significant role in PDL development and homeostasis, which requires additional investigations.

We hope our study is opening a new gateway and molecular clues for understanding how the PDL, one of the most dynamically changed tissues in the body, is maintained for homeostasis and integrity, not only in physiological conditions, but also for periodontal diseases.

### Acknowledgement

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### Material and data availability statement

The materials used and datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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**Figure legends**

**Figure 1. PDL express distinct molecular signatures upon occlusion establishment**

A: Hematoxylin-Eosin (HE) staining of the P18 and P28 rat first lower molar.

B: Goldner staining of P18 and P28 PDL regions. Note the green-blue stained collagen fibers are abundant at P28 but not P18.

C: Immunofluorescent staining of Periostin with a specific antibody raised in rabbit then visualised using anti-Rabbit Alexa 568 (red) conjugated secondary antibody. Note the significantly increased Periostin signal at P28 comparing to P18.

D: Gene function enrichment analysis on the RNAseq results by comparing P28 with P18 PDL.

E, F: Differential analysis performed on the RNAseq results by comparing P28 with P18 PDL.

E: Metacore Pathway Maps heatmaps analysis.

D: GO analysis for the biological processes.

Bars: A: 100µm; B, C: 20µm.

**Figure 2. Notch signalling has dynamic changes during PDL maturation**

A: String analysis of the genes of top 10 pathways of the metacore Pathway Maps of the RNAseq results.

B: Metacore Pathway Maps analysis.

C: String analysis of the genes of top 10 pathways of the metacore Pathway Maps.

D: Notch pathway members that had significant changes in the RNAseq analysis.

D-H: Immunofluorescent analysis of the indicated molecules using specific primary antibodies. The Alexa 488 (green) or 568 (red) conjugated secondaries were used to identify the primary antibodies. Dotted lines mark the boundary between PDL and bone (B) or dentin (D).

Bars: 20 $\mu$ m

### Figure 3. Intercepting canonical Notch pathway delayed PDL maturation

A: Immunostaining PDL of the second lower molars from P21 RBP-Jk<sup>flox/flox</sup> (control) and Collagen 1a2 Cre x RBP-Jk<sup>flox/flox</sup> (cKO) mice. Note the Cre positive signal could only be observed in the cKO mice.

B: HE staining of the P21 control and cKO mice second lower molars. Stars: PDL.

C, D: Stereo images of 1 month old control and cKO mouse mandibles and first lower molars. Note the cKO mouse tooth's crown size are smaller and roots are shorter than the control.

E: Representative stereo images of the first and third lower molars of the control and cKO mice at postnatal day 14.

F: Representative micro-CT analysis of the control and cKO first lower molar eruption from 4 months old animals.

G: First lower molar mesial buccal root length comparison at P14 and 2 months. \*\*  $p < 0.01$ .

H-J: Immunofluorescent analysis of Periostin using specific primary followed by secondary antibodies (Alexa 568, red) at indicated stages. Note comparing to the controls, RBP-Jkappa cKO mouse PDL has delayed expression of Periostin at P10 and P14, but not at 2 months.

Bars: A, B, H-J: 20 $\mu$ m; C-F: 1mm.

### Figure 4. Stretching force induced *Notch* pathway activation and matrix protein productions on a human PDL cell line.



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A and B: Real time RT-PCR analysis on human PDL cells at a ratio of 20% stretching and frequency of 30x/min. Samples were collected after 12 hours. \*\* p<0.01.

C: Metacore analysis of proteomic analysis on the samples of A and B.

D: String analysis of the top 5 pathways affected by stretching force.

**Figure 5. Lamin A is a marker of PDL maturation and is under the control of Notch pathway.**

A: Compound analysis of the common targets from the *in vivo* RNAseq (Figure 1) and proteomic and *in vitro* cell stretching results (Figure 4). Note Lamin A (LMNA) is the only molecule that was commonly regulated in the three conditions.

B: Immunofluorescent analysis of Lamin A/C expression in the P18 vs. P28 PDL. D: Dentin; B: Bone; Dotted lines: boundaries.

C: Western blotting analysis of Lamin A/C expression in the human PDL cells upon stretching (Figure 4 A&B), with GapDH as the loading control. Note only Lamin A expression was significantly changed.

D: Western blotting analysis of Lamin A/C expression in the human PDL cells treated with Jagged1, with GapDH as the loading control. Note again only Lamin A expression was significantly changed.

E and F: Immunofluorescent analysis of Lamin A/C expression in the control and cKO mouse PDL at P10 and 2 months. D: Dentin; B: Bone; Dotted lines: boundaries.

Bars: 20µm

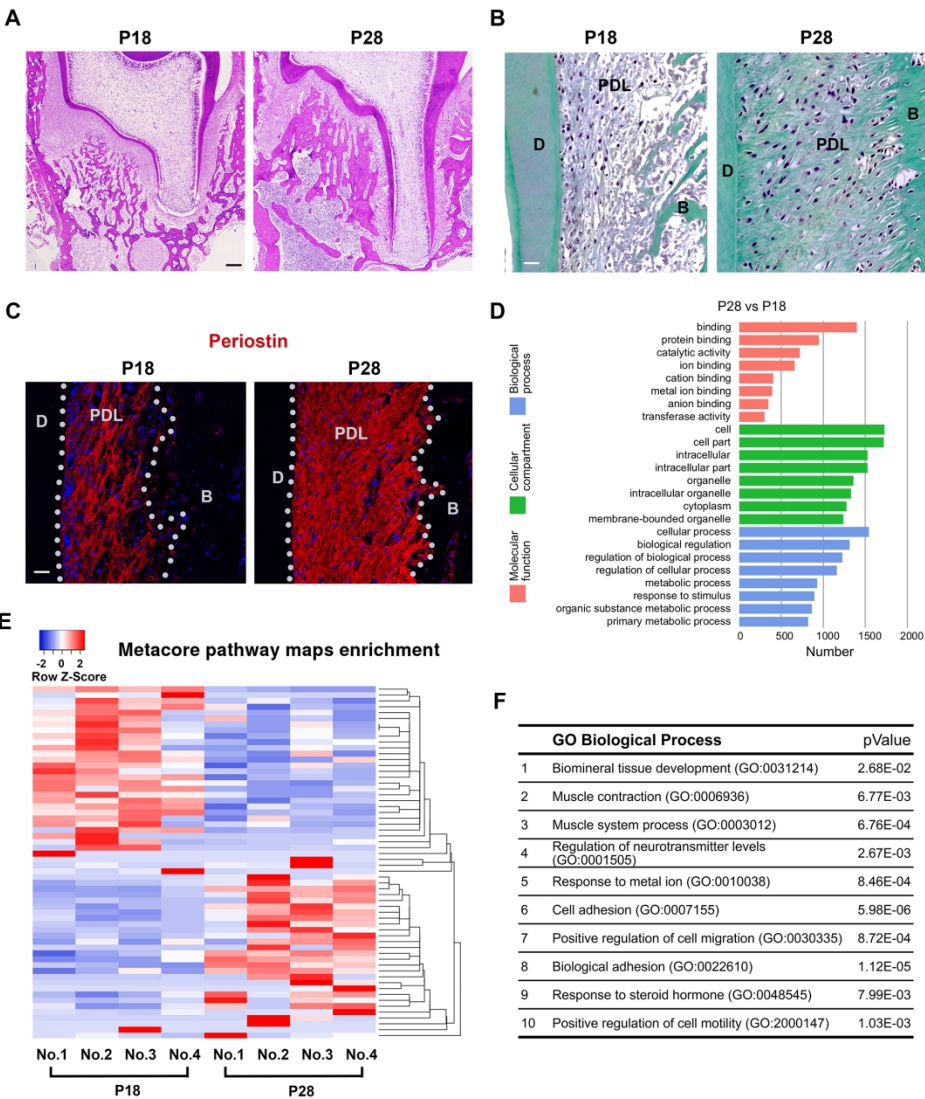


Figure 1

182x227mm (300 x 300 DPI)

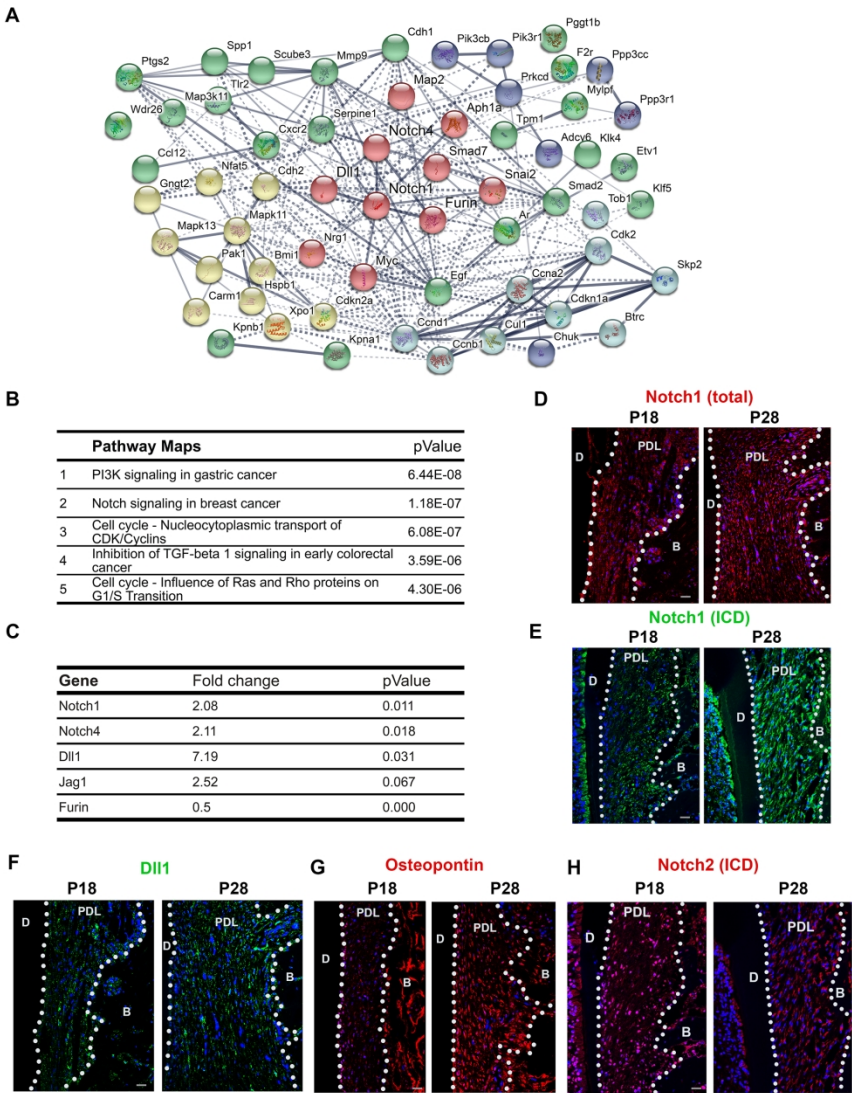


Figure 2

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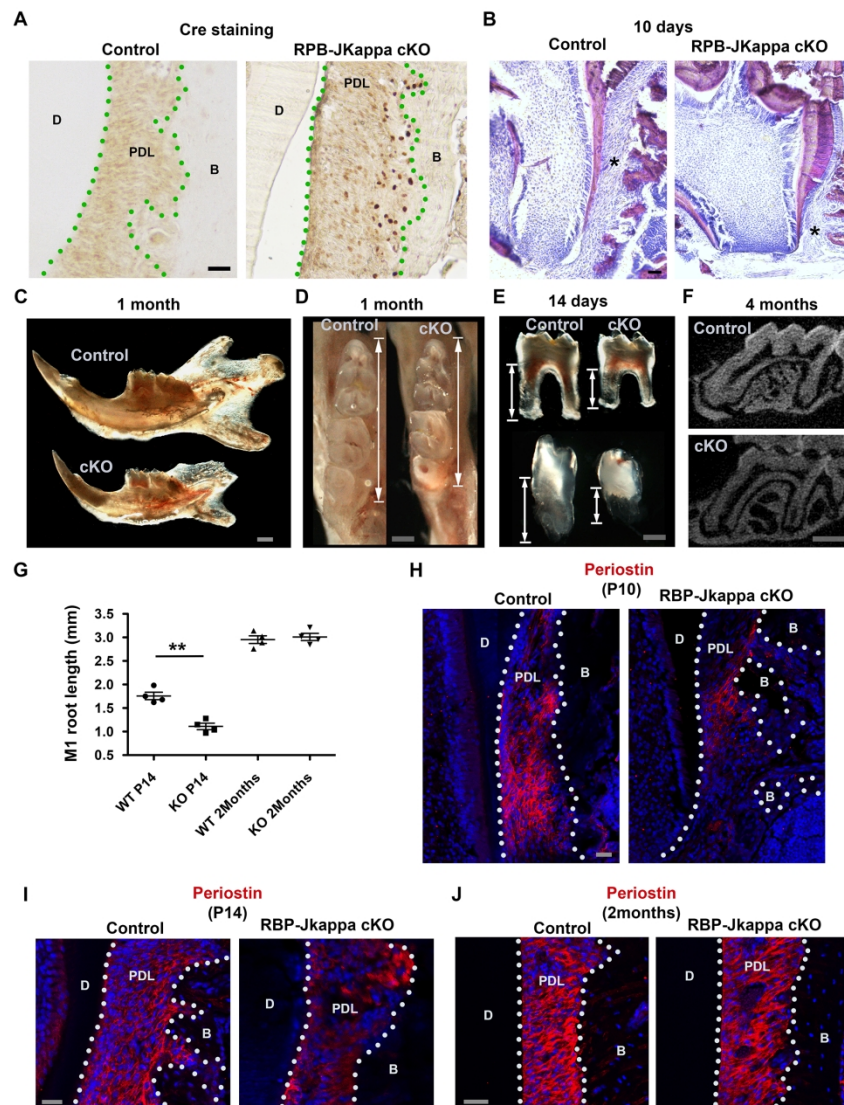


Figure 3

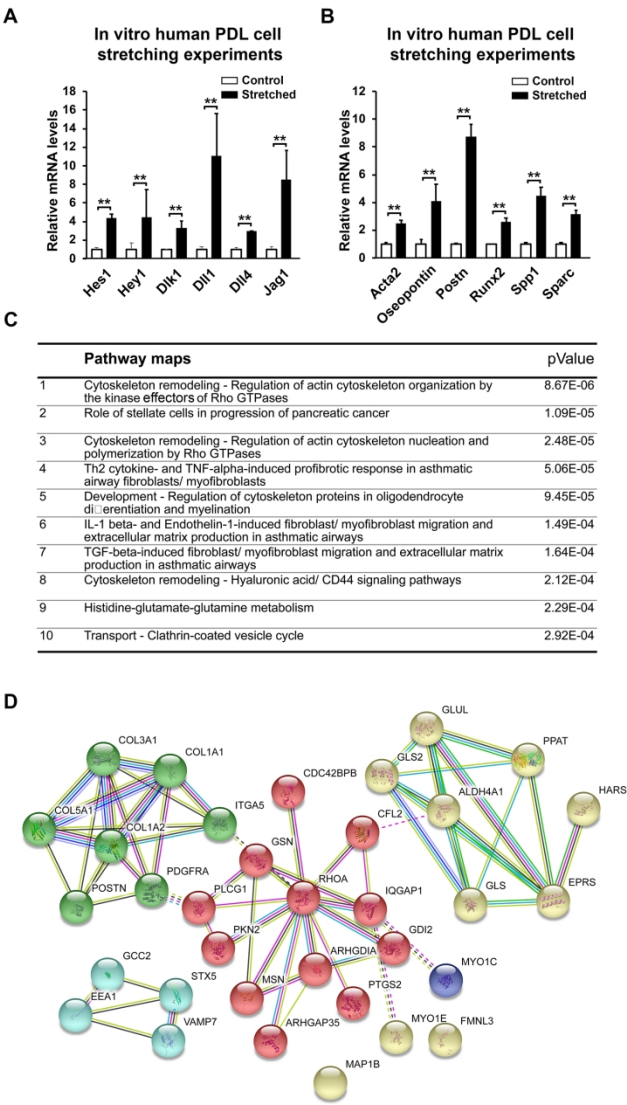


Figure 4



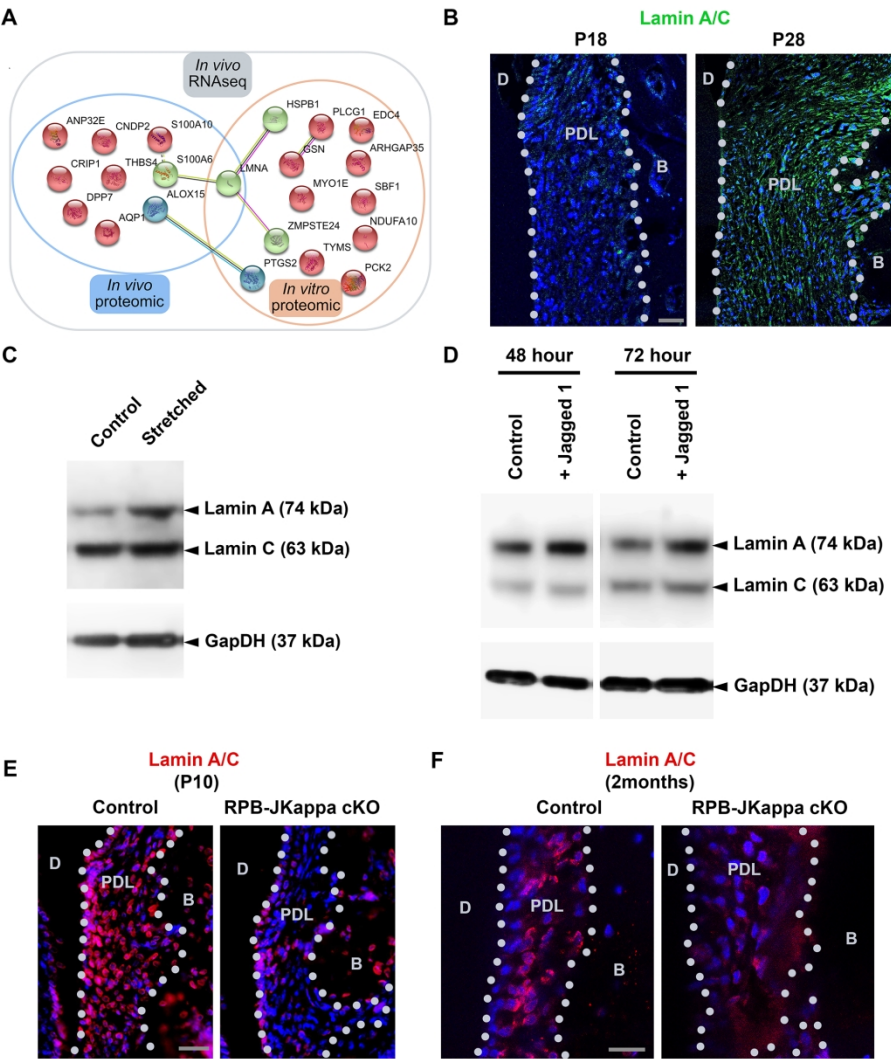


Figure 5

176x227mm (300 x 300 DPI)

**Notch coordinates periodontal ligament maturation through regulating Lamin A**

Balazs Jozsef Denes<sup>1</sup>, Chloe Bolton<sup>2</sup>, Charlotte Sara Illsley<sup>2</sup>, Wai Ling Kok<sup>2</sup>, Jemma Victoria Walker<sup>2</sup>, Ansgar Poetsch<sup>3</sup>, Christopher Tredwin<sup>2</sup>, Stavros Kiliaridis<sup>1</sup>, Bing Hu<sup>2\*</sup>

**Appendix files and legends**

**Appendix Figure 1**

A: Additional micro-CT analysis on P18 and P28 rat root.  
B: Additional process network analysis on the RNAseq results illustrated in Figure 1.  
Bar: 100µm

**Appendix Figure 2**

A: Periostin expression analysis at postnatal day 4 (P4) in the control and RBP-Jkappa cKO mice.  
B: The stretching device system used in this study.  
Bar: 20µm

**Appendix Figure 3**

Summarisation of the findings of study and perspectives.

**Appendix Table 1**

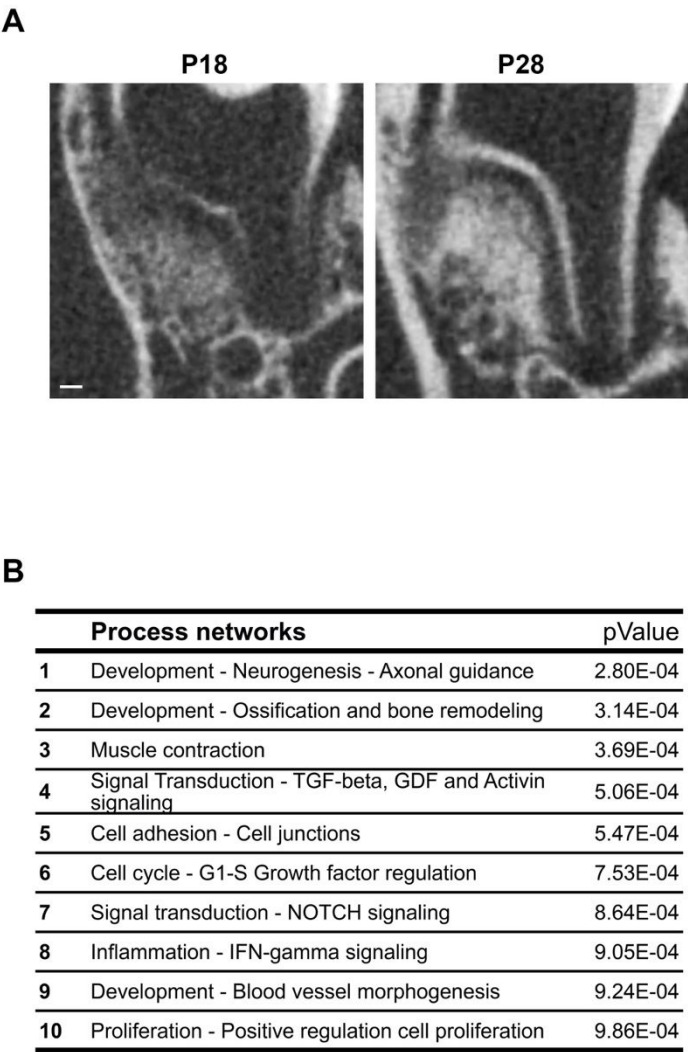
The RNAseq summary of the study.

**Appendix Table 2**

The original proteomic analysis data of stretched PDL cells showed in Figure 4.

Appendix Table 3

The antibodies, primers and protein used in the study.

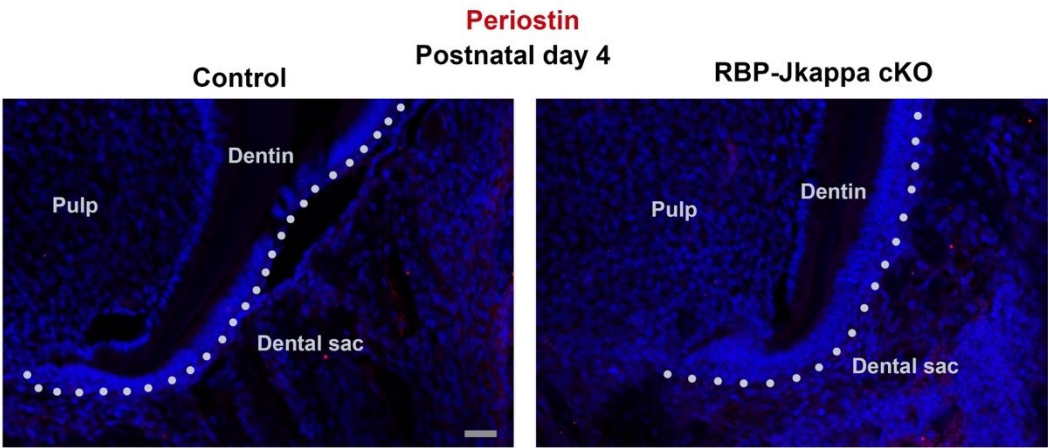


Appendix Figure 1



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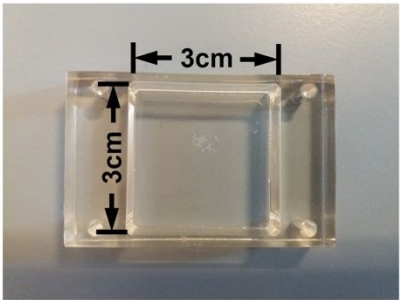


B



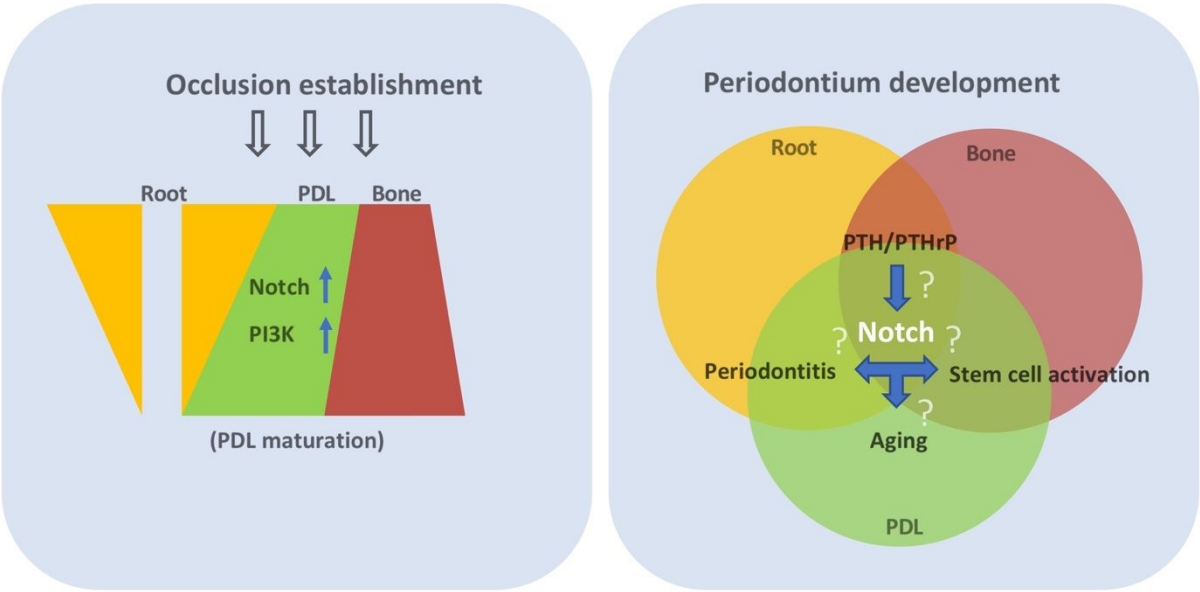
Stretching unit Controlling unit

C



Stretching chamber

Appendix Figure 2



Appendix Figure 3

Review

Appendix Table 1

Summary of the fold changes of the genes up and down regulated comparing P28 with P18 PDL based on the RNAseq analysis results as showed in Figure 1D. The genes inside the category of “Cell” has been shown as below.

<i>A4galt</i>	56.2	0.012
<i>Aak1</i>	-6.2	0.046
<i>Aatf</i>	-3.0	0.001
<i>Abca2</i>	4.4	0.001
<i>Abca4</i>	-27.3	0.034
<i>Abca7</i>	5.6	0.036
<i>Abcc2</i>	-29.1	0.037
<i>Abcc5</i>	2.9	0.006
<i>Abcd3</i>	2.5	0.023
<i>Abce1</i>	-2.0	0.001
<i>Abi1</i>	1.7	0.008
<i>Abi3</i>	2.6	0.005
<i>Abt1</i>	1.5	0.046
<i>Acads</i>	1.6	0.038
<i>Acbd3</i>	2.1	0.032
<i>Acer1</i>	60.2	0.042
<i>Ache</i>	-10.8	0.013
<i>Ache</i>	-10.8	0.013
<i>Ackr2</i>	840.3	0.003
<i>Ackr3</i>	2.7	0.006
<i>Acot11</i>	-122.2	0.039
<i>Acox1</i>	-5.4	0.016
<i>Acp5</i>	12.7	0.001
<i>Acsbg1</i>	77.1	0.038
<i>Acta2</i>	-4.2	0.004
<i>Actr10</i>	-1.6	0.022
<i>Actr3</i>	-1.9	0.017
<i>Acvr1b</i>	24.5	0.044
<i>Adam19</i>	-1.8	0.044
<i>Adamts15</i>	32.3	0.036
<i>Adcy10</i>	89.7	0.015
<i>Adcy6</i>	2.4	0.029
<i>Adcyap1r1</i>	23.1	0.022
<i>Adh4</i>	16.2	0.046
<i>Adh5</i>	-1.5	0.020
<i>Adh6a</i>	-126.0	0.020
<i>Adh7</i>	1517.8	0.003
<i>Adm</i>	-10.4	0.000
<i>Adpgk</i>	-1.6	0.016

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2	<i>Adra1b</i>	28.5	0.032
3	<i>Adrb1</i>	-59.2	0.048
4	<i>Adsl</i>	-1.9	0.003
5	<i>Afg3l2</i>	-1.7	0.048
6	<i>Aga</i>	1.7	0.009
7	<i>Agpat4</i>	-2.3	0.002
8	<i>Agps</i>	-2.9	0.042
9	<i>Ahnak</i>	2.2	0.032
10	<i>Aif1l</i>	-8.4	0.016
11	<i>Ak1</i>	-1.9	0.015
12	<i>Akap12</i>	2.2	0.018
13	<i>Akap17a</i>	2.6	0.021
14	<i>Akap5</i>	-158.1	0.017
15	<i>Akap8l</i>	2.4	0.001
16	<i>Akip1</i>	1.9	0.013
17	<i>Alad</i>	-1.8	0.045
18	<i>Alas2</i>	-5.7	0.012
19	<i>Aldh1a3</i>	-73.2	0.017
20	<i>Aldh1b1</i>	-159.0	0.002
21	<i>Aldh1l1</i>	-9.6	0.031
22	<i>Aldh6a1</i>	-1.8	0.013
23	<i>Alg11</i>	-3.1	0.000
24	<i>Alg2</i>	-2.6	0.004
25	<i>Alk</i>	339.8	0.006
26	<i>Alox15</i>	-11.1	0.001
27	<i>Als2</i>	-11.3	0.032
28	<i>Amelx</i>	-88.0	0.006
29	<i>Amigo1</i>	-147.1	0.025
30	<i>Ampd1</i>	60.5	0.011
31	<i>Amph</i>	-19.5	0.036
32	<i>Anapc1</i>	-1.7	0.033
33	<i>Anapc5</i>	-1.6	0.001
34	<i>Angptl6</i>	49.7	0.023
35	<i>Ankhd1</i>	2.1	0.011
36	<i>Ankrd13a</i>	-1.8	0.010
37	<i>Ankrd23</i>	22.9	0.036
38	<i>Anp32e</i>	-2.7	0.000
39	<i>Aox3</i>	31.0	0.032
40	<i>Ap1s2</i>	-1.7	0.026
41	<i>Ap2m1</i>	-1.7	0.003
42	<i>Aph1a</i>	-2.3	0.001
43	<i>Api5</i>	-1.7	0.004
44	<i>Apoc3</i>	55.0	0.011
45	<i>Aqp1</i>	2.7	0.015
46	<i>Aqp3</i>	211.9	0.001
47	<i>Aqp4</i>	1752.4	0.001
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2	Ar	20.5	0.005
3	Ar	20.5	0.005
4	Ar	20.5	0.005
5	Ar	20.5	0.005
6	Arcn1	-1.9	0.001
7	Arf1	-1.8	0.021
8	Arf2	-1.9	0.017
9	Arf4	-1.5	0.004
10	Arfip1	-2.6	0.007
11	Arfip2	2.3	0.003
12	Arg2	5.8	0.000
13	Arglu1	2.0	0.028
14	Arhgap35	1.9	0.047
15	Arhgap4	-4.8	0.027
16	Arhgef18	-1.9	0.037
17	Arhgef25	-1.8	0.013
18	Arhgef7	-1.7	0.037
19	Arl1	-2.6	0.001
20	Arl3	1.6	0.015
21	Arl6ip1	-1.6	0.050
22	Arntl	2.3	0.025
23	Arntl2	-85.0	0.036
24	Arrdc1	1.6	0.009
25	Arsi	7.2	0.019
26	Asgr2	178.3	0.002
27	Ash1l	2.0	0.039
28	Asic1	79.2	0.023
29	Asip	71.8	0.027
30	Atad1	-2.0	0.021
31	Ate1	1.9	0.016
32	Atf4	1.6	0.012
33	Atic	-2.8	0.000
34	Atl2	-4.1	0.031
35	Atoh8	3.6	0.001
36	Atp1a3	-52.7	0.032
37	Atp2a2	-1.6	0.010
38	Atp2b2	98.2	0.013
39	Atp2b3	36.5	0.049
40	Atp2b4	1.9	0.038
41	Atp5e	2.0	0.030
42	Atp5i	1.7	0.039
43	Atp5j2	1.7	0.029
44	Atp6v0b	2.4	0.001
45	Atp6v1e1	1.7	0.005
46	Atp6v1e2	164.2	0.017
47	Atp6v1f	1.8	0.001
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2	<i>Atxn10</i>	-2.2	0.000
3	<i>Avil</i>	417.1	0.000
4	<i>Avp</i>	183.0	0.008
5	<i>Azin2</i>	5.5	0.028
6	<i>B2m</i>	2.0	0.002
7	<i>B3galnt1</i>	-1.6	0.040
8	<i>B3galt1</i>	-264.1	0.037
9	<i>B3galt2</i>	-43.4	0.012
10	<i>B3galt6</i>	-3.0	0.018
11	<i>B3gat3</i>	1.9	0.001
12	<i>B4galnt4</i>	-13.4	0.047
13	<i>B4galt2</i>	-1.6	0.014
14	<i>B4galt6</i>	1.9	0.008
15	<i>B9d2</i>	1.8	0.013
16	<i>Bag3</i>	1.8	0.042
17	<i>Bag4</i>	-4.3	0.031
18	<i>Batf</i>	3.3	0.017
19	<i>Bbs2</i>	-2.0	0.043
20	<i>Bche</i>	-122.2	0.031
21	<i>Bckdhh</i>	-1.9	0.003
22	<i>Bcl2l15</i>	42.5	0.050
23	<i>Bcl6</i>	4.9	0.002
24	<i>Bcorl1</i>	2.4	0.034
25	<i>Bglap</i>	4.6	0.003
26	<i>Blk</i>	-17.9	0.002
27	<i>Bloc1s1</i>	1.6	0.037
28	<i>Blzf1</i>	-2.2	0.036
29	<i>Bmi1</i>	-7.3	0.013
30	<i>Bmpr1a</i>	-3.8	0.006
31	<i>Bmx</i>	-30.0	0.013
32	<i>Bod1</i>	1.6	0.028
33	<i>Brd9</i>	1.7	0.043
34	<i>Brf1</i>	-1.7	0.037
35	<i>Bri3</i>	2.4	0.009
36	<i>Brinp1</i>	-42.1	0.000
37	<i>Brinp2</i>	121.9	0.003
38	<i>Brms1l</i>	-4.0	0.006
39	<i>Btaf1</i>	1.7	0.046
40	<i>Btbd1</i>	-1.7	0.009
41	<i>Btbd6</i>	-1.7	0.010
42	<i>Btk</i>	-7.5	0.014
43	<i>Btnl2</i>	-63.2	0.022
44	<i>Btrc</i>	-2.8	0.015
45	<i>Bub1</i>	-2.7	0.013
46	<i>Bzw1</i>	-2.2	0.011
47	<i>Bzw2</i>	-2.0	0.001
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2	<i>C1qa</i>	2.5	0.003
3	<i>C1qb</i>	1.9	0.041
4	<i>C1qc</i>	1.9	0.042
5	<i>Cacna1c</i>	-4.9	0.004
6	<i>Cacna2d4</i>	30.2	0.045
7	<i>Cacnb4</i>	74.6	0.018
8	<i>Cacng6</i>	-137.5	0.026
9	<i>Cadm1</i>	4.0	0.003
10	<i>Calb1</i>	-39.7	0.008
11	<i>Calcb</i>	-65.3	0.023
12	<i>Calm3</i>	-1.5	0.037
13	<i>Camk1g</i>	146.8	0.018
14	<i>Camk2a</i>	-34.6	0.047
15	<i>Camk2d</i>	-4.3	0.031
16	<i>Capg</i>	2.9	0.001
17	<i>Capn12</i>	4.9	0.005
18	<i>Capn15</i>	2.6	0.026
19	<i>Capn3</i>	-348.3	0.001
20	<i>Caprin1</i>	-2.1	0.002
21	<i>Capza1</i>	-1.9	0.002
22	<i>Capza2</i>	-1.6	0.014
23	<i>Carf</i>	15.0	0.025
24	<i>Carm1</i>	-2.1	0.017
25	<i>Casp1</i>	-4.0	0.017
26	<i>Casp4</i>	3.4	0.006
27	<i>Casp7</i>	-3.6	0.008
28	<i>Casp8</i>	-11.9	0.000
29	<i>Cav3</i>	72.1	0.044
30	<i>Cbl1</i>	1.9	0.003
31	<i>Cbx7</i>	7.3	0.049
32	<i>Ccar1</i>	1.7	0.035
33	<i>Ccdc22</i>	3.9	0.024
34	<i>Ccdc67</i>	-170.7	0.012
35	<i>Ccdc69</i>	-20.1	0.032
36	<i>Cchcr1</i>	1.8	0.020
37	<i>Ccl12</i>	112.4	0.015
38	<i>Ccl21</i>	258.3	0.014
39	<i>Ccna2</i>	-3.1	0.006
40	<i>Ccnb1</i>	-2.1	0.026
41	<i>Ccnb1ip1</i>	427.6	0.003
42	<i>Ccnd1</i>	2.1	0.025
43	<i>Ccndbp1</i>	1.9	0.004
44	<i>Ccnh</i>	-1.7	0.015
45	<i>Ccny</i>	-1.9	0.042
46	<i>Ccr7</i>	44.0	0.046
47	<i>Cct6a</i>	-1.6	0.011
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<i>Cd164</i>	-1.8	0.001
<i>Cd177</i>	-22.0	0.027
<i>Cd19</i>	-64.0	0.004
<i>Cd22</i>	-97.8	0.002
<i>Cd244</i>	-34.9	0.016
<i>Cd320</i>	1.8	0.008
<i>Cd36</i>	-10.9	0.017
<i>Cd38</i>	-22.3	0.027
<i>Cd3g</i>	-10.1	0.032
<i>Cd44</i>	1.9	0.029
<i>Cd5</i>	92.0	0.023
<i>Cd55</i>	17.0	0.009
<i>Cd68</i>	3.0	0.013
<i>Cd69</i>	-569.3	0.003
<i>Cd79b</i>	-6.2	0.017
<i>Cd9</i>	2.3	0.000
<i>Cd99</i>	2.0	0.014
<i>Cdc123</i>	-1.7	0.005
<i>Cdc14a</i>	3.2	0.013
<i>Cdc16</i>	-2.2	0.000
<i>Cdc23</i>	-2.0	0.011
<i>Cdc26</i>	-2.7	0.000
<i>Cdc34</i>	1.7	0.026
<i>Cdc40</i>	-1.8	0.028
<i>Cdc6</i>	-4.8	0.015
<i>Cdca7</i>	-3.2	0.011
<i>Cdh1</i>	8.6	0.046
<i>Cdh13</i>	2.5	0.002
<i>Cdh17</i>	62.4	0.004
<i>Cdh2</i>	2.9	0.031
<i>Cdk2</i>	-2.1	0.047
<i>Cdk2ap2</i>	1.9	0.001
<i>Cdk5</i>	2.3	0.001
<i>Cdkn1a</i>	5.1	0.004
<i>Cdkn2a</i>	-71.7	0.035
<i>Cdkn2aip, Carf</i>	#N/A	#N/A
<i>Cdnf</i>	273.1	0.012
<i>Cdv3</i>	2.1	0.020
<i>Cebpd</i>	-1.8	0.029
<i>Cers3</i>	67.1	0.031
<i>Cfap126</i>	-129.8	0.019
<i>Cgnl1</i>	7.2	0.001
<i>Chchd10</i>	5.9	0.041
<i>Chi3l1</i>	-17.2	0.006
<i>Chp1</i>	-2.0	0.036
<i>Chpf2</i>	-1.7	0.016



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2	<i>Chrna4</i>	-12.6	0.022
3	<i>Chrnbl</i>	53.6	0.011
4	<i>Chst11</i>	11.2	0.039
5	<i>Chst12</i>	-1.7	0.035
6	<i>Chuk</i>	-2.3	0.011
7	<i>Cidea</i>	-247.0	0.012
8	<i>Cideb</i>	-27.2	0.032
9	<i>Cited1</i>	-39.0	0.035
10	<i>Cited2</i>	1.9	0.011
11	<i>Ckb</i>	2.1	0.024
12	<i>Cks2</i>	1.8	0.037
13	<i>Clca5</i>	155.2	0.008
14	<i>Clcn3</i>	-3.8	0.031
15	<i>Cldn10</i>	-443.2	0.001
16	<i>Cldn20</i>	-229.9	0.009
17	<i>Cldnd1</i>	-2.0	0.000
18	<i>Clip4</i>	24.3	0.048
19	<i>Clk1</i>	2.7	0.001
20	<i>Cln3</i>	2.9	0.013
21	<i>Cln8</i>	-2.8	0.011
22	<i>Clock</i>	2.6	0.030
23	<i>Clstn1</i>	1.7	0.049
24	<i>Clstn3</i>	424.9	0.001
25	<i>Clu</i>	-1.9	0.018
26	<i>Clvs1</i>	1.9	0.042
27	<i>Clvs2</i>	-76.4	0.041
28	<i>Cmc1</i>	2.1	0.006
29	<i>Cmpk1</i>	-1.7	0.001
30	<i>Cndp2</i>	-2.7	0.002
31	<i>Cnep1r1</i>	-2.2	0.026
32	<i>Cnih2</i>	-2.8	0.018
33	<i>Cnn3</i>	-1.6	0.016
34	<i>Cnot10</i>	2.1	0.003
35	<i>Cnp</i>	-1.8	0.016
36	<i>Cnp</i>	-1.8	0.016
37	<i>Cnrip1</i>	-1.7	0.032
38	<i>Cntf</i>	25.6	0.000
39	<i>Cntn1</i>	115.3	0.009
40	<i>Cntn6</i>	361.2	0.003
41	<i>Cntnap4</i>	1391.6	0.001
42	<i>Coa4</i>	2.0	0.007
43	<i>Coasy</i>	1.9	0.039
44	<i>Cog4</i>	-1.5	0.021
45	<i>Cog6</i>	-4.5	0.041
46	<i>Cog7</i>	-2.2	0.017
47	<i>Col26a1</i>	-3.6	0.017
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2	<i>Col4a3bp</i>	3.3	0.028
3	<i>Col6a2</i>	2.0	0.007
4	<i>Commd4</i>	1.9	0.003
5	<i>Copg1</i>	-2.1	0.022
6	<i>Coprs</i>	1.9	0.014
7	<i>Cops4</i>	-2.1	0.001
8	<i>Copz1</i>	-1.5	0.004
9	<i>Coq10b</i>	-2.1	0.028
10	<i>Coro1a</i>	-3.0	0.017
11	<i>Coro2a</i>	144.1	0.004
12	<i>Cotl1</i>	-1.7	0.021
13	<i>Cox17</i>	1.9	0.012
14	<i>Cox20</i>	1.7	0.029
15	<i>Cox7b</i>	2.0	0.013
16	<i>Cpeb1</i>	276.3	0.015
17	<i>Cpne9</i>	33.9	0.026
18	<i>Cpq</i>	1.6	0.032
19	<i>Cpsf4</i>	-2.1	0.038
20	<i>Cpt1c</i>	3.3	0.037
21	<i>Cr2</i>	-201.2	0.009
22	<i>Creb3l4</i>	186.5	0.009
23	<i>Crebbp</i>	1.7	0.049
24	<i>Crip1</i>	2.5	0.002
25	<i>Crip2</i>	1.7	0.009
26	<i>Crlf3</i>	-4.8	0.003
27	<i>Crls1</i>	-2.0	0.023
28	<i>Crtac1</i>	49.4	0.020
29	<i>Cs</i>	-1.8	0.010
30	<i>Csf2ra</i>	3.7	0.000
31	<i>Csnk1d</i>	-1.6	0.003
32	<i>Cspg4</i>	2.8	0.012
33	<i>Csrp2</i>	-1.7	0.033
34	<i>Cst3</i>	2.9	0.000
35	<i>Cstb</i>	1.8	0.021
36	<i>Cstf1</i>	-2.7	0.000
37	<i>Cstf2</i>	-2.8	0.045
38	<i>Ctbs</i>	1.7	0.042
39	<i>Ctdsp1</i>	1.8	0.002
40	<i>Ctdspl2</i>	-2.4	0.024
41	<i>Ctif</i>	33.6	0.034
42	<i>Ctps1</i>	-2.5	0.000
43	<i>Ctrb1</i>	98.1	0.013
44	<i>Ctsc</i>	-2.7	0.008
45	<i>Ctsd</i>	1.7	0.001
46	<i>Ctse</i>	-26.6	0.000
47	<i>Ctsf</i>	1.7	0.021
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2	<i>Ctsw</i>	-76.8	0.003
3	<i>Ctsz</i>	3.6	0.004
4	<i>Cuedc2</i>	1.6	0.029
5	<i>Cul1</i>	-2.9	0.000
6	<i>Cul2</i>	-1.8	0.049
7	<i>Cul3</i>	-1.6	0.018
8	<i>Cxcl1</i>	305.7	0.011
9	<i>Cxcl10</i>	136.2	0.021
10	<i>Cxcl14</i>	-2.0	0.044
11	<i>Cxcr2</i>	-43.8	0.035
12	<i>Cxcr3</i>	30.2	0.042
13	<i>Cxcr6</i>	-226.8	0.025
14	<i>Cyb5b</i>	-1.6	0.034
15	<i>Cyba</i>	1.7	0.018
16	<i>Cyfp2</i>	-7.9	0.002
17	<i>Cyp27a1</i>	9.7	0.038
18	<i>Cyp27b1</i>	163.4	0.019
19	<i>Cyp2j10</i>	220.6	0.001
20	<i>Cyp2r1</i>	45.8	0.022
21	<i>Cyp39a1</i>	283.3	0.005
22	<i>Cyp3a9</i>	92.3	0.031
23	<i>Cyp4b1</i>	206.1	0.008
24	<i>Cyp7b1</i>	-5.8	0.003
25	<i>Cysltr1</i>	-103.8	0.039
26	<i>Dab2</i>	-1.7	0.027
27	<i>Dab2ip</i>	1.9	0.016
28	<i>Dapk1</i>	2.0	0.023
29	<i>Dars</i>	-2.4	0.013
30	<i>Dbf4</i>	-3.8	0.039
31	<i>Dbn1</i>	-1.5	0.045
32	<i>Dcaf8</i>	-1.8	0.002
33	<i>Dcdc2</i>	93.5	0.031
34	<i>Dcps</i>	-2.6	0.008
35	<i>Dcxr</i>	2.2	0.010
36	<i>Ddx46</i>	1.6	0.027
37	<i>Ddx50</i>	-1.6	0.037
38	<i>Ddx58</i>	3.8	0.022
39	<i>Ddx59</i>	2.1	0.025
40	<i>Dffa</i>	2.2	0.005
41	<i>Dgkg</i>	-15.8	0.028
42	<i>Dgki</i>	298.6	0.000
43	<i>Dhcr24</i>	-35.7	0.002
44	<i>Dhps</i>	-2.1	0.002
45	<i>Dhrs7c</i>	145.1	0.018
46	<i>Dhx30</i>	2.1	0.006
47	<i>Dhx8</i>	-2.6	0.013
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<i>Dkk1</i>	-98.4	0.045
<i>Dlgap4</i>	2.1	0.002
<i>Dll1</i>	7.2	0.031
<i>Dnaja3</i>	-1.8	0.043
<i>Dnajib13</i>	263.7	0.002
<i>Dnajib4</i>	-2.1	0.016
<i>Dnajib6</i>	-2.1	0.015
<i>Dnajc16</i>	-900.3	0.000
<i>Dnase1l1</i>	2.9	0.011
<i>Dnase1l3</i>	-299.8	0.002
<i>Dnase2</i>	1.9	0.001
<i>Dnase2b</i>	44.0	0.019
<i>Dnlz</i>	1.9	0.021
<i>Dnm3</i>	-3.3	0.043
<i>Dock8</i>	-4.2	0.028
<i>Dock9</i>	2.9	0.034
<i>Dpep1</i>	29.8	0.039
<i>Dpf1</i>	92.0	0.001
<i>Dph3</i>	1.6	0.033
<i>Dpp4</i>	-19.8	0.004
<i>Dpp7</i>	1.8	0.010
<i>Dpyd</i>	84.5	0.003
<i>Dpysl2</i>	2.1	0.018
<i>Dram2</i>	-1.9	0.026
<i>Drg1</i>	-2.3	0.006
<i>Dsc3</i>	91.8	0.005
<i>Dsg3</i>	21.5	0.038
<i>Duox1</i>	3.7	0.011
<i>Dusp10</i>	-2.6	0.048
<i>Dusp3</i>	1.9	0.005
<i>Dusp4</i>	-33.4	0.038
<i>Dvl1</i>	2.1	0.012
<i>Dym</i>	-2.0	0.011
<i>Dync1i2</i>	1.5	0.047
<i>Dyrk2</i>	2.0	0.009
<i>Eaf2</i>	-36.5	0.041
<i>Edar</i>	-74.6	0.045
<i>Edc4</i>	2.1	0.003
<i>Eef1a1</i>	-1.9	0.018
<i>Eef1e1</i>	-2.1	0.003
<i>Efemp1</i>	5.1	0.037
<i>Egf</i>	22.1	0.036
<i>Egfl7</i>	1.9	0.012
<i>Egr2</i>	653.0	0.001
<i>Ehf</i>	187.0	0.020
<i>Ehmt1</i>	-5.3	0.001

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2	<i>Ei24</i>	-2.2	0.000
3	<i>Eif2b1</i>	-1.6	0.011
4	<i>Eif2b3</i>	-2.5	0.003
5	<i>Eif2s1</i>	-1.6	0.018
6	<i>Eif4a1</i>	-1.5	0.002
7	<i>Eif4e</i>	-1.6	0.025
8	<i>Elf1</i>	-2.8	0.016
9	<i>Elf4</i>	-8.8	0.042
10	<i>Elov14</i>	-6.4	0.012
11	<i>Elov15</i>	-3.4	0.045
12	<i>Emc4</i>	1.7	0.002
13	<i>Emd</i>	2.1	0.020
14	<i>Emid1</i>	-2.9	0.000
15	<i>Eml1</i>	-3.1	0.020
16	<i>Enc1</i>	-3.1	0.010
17	<i>Enoph1</i>	-2.0	0.028
18	<i>Enpp1</i>	-2.5	0.018
19	<i>Enpp2</i>	3.1	0.020
20	<i>Enpp6</i>	130.7	0.001
21	<i>Eogt</i>	-23.6	0.015
22	<i>Epc1</i>	2.5	0.046
23	<i>Epha1</i>	233.9	0.003
24	<i>Epha2</i>	2.1	0.009
25	<i>Erh</i>	-1.6	0.001
26	<i>Espn</i>	30.6	0.008
27	<i>Esrp1</i>	73.2	0.017
28	<i>Esrp2</i>	130.5	0.025
29	<i>Etf1</i>	-1.5	0.030
30	<i>Etv1</i>	3.9	0.032
31	<i>Eva1a</i>	-1.8	0.027
32	<i>Evpl</i>	203.0	0.010
33	<i>Exoc6b</i>	-3.4	0.003
34	<i>Ezh1</i>	3.7	0.009
35	<i>F11r</i>	-1.8	0.047
36	<i>F12</i>	-154.6	0.010
37	<i>F2r</i>	-2.8	0.001
38	<i>Fa2h</i>	25.3	0.037
39	<i>Fabp5</i>	2.7	0.015
40	<i>Fah</i>	5.6	0.007
41	<i>Fam118b</i>	-2.1	0.045
42	<i>Fam126a</i>	-22.4	0.000
43	<i>Fam126b</i>	4.2	0.035
44	<i>Fam161a</i>	-82.9	0.016
45	<i>Fam172a</i>	-2.0	0.025
46	<i>Fam20c</i>	3.1	0.003
47	<i>Fam26e</i>	-15.4	0.041
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2	<i>Fam26f</i>	25.2	0.039
3	<i>Fam46c</i>	-2.4	0.032
4	<i>Fam65a</i>	1.9	0.010
5	<i>Fam96b</i>	1.7	0.010
6	<i>Fam98c</i>	1.7	0.021
7	<i>Fanca</i>	4.9	0.003
8	<i>Farsb</i>	-3.9	0.000
9	<i>Fasn</i>	1.7	0.039
10	<i>Fat1</i>	2.3	0.036
11	<i>Fbxl4</i>	-4.1	0.024
12	<i>Fbxl5</i>	-1.7	0.042
13	<i>Fbxo2</i>	204.6	0.026
14	<i>Fbxo39</i>	42.3	0.042
15	<i>Fbxo44</i>	214.6	0.016
16	<i>Fbxo7</i>	-2.0	0.033
17	<i>Fcmr</i>	-5.2	0.020
18	<i>Fcnb</i>	-13.2	0.012
19	<i>Fcrla</i>	-6.4	0.049
20	<i>Fdx1</i>	1.6	0.010
21	<i>Fem1a</i>	1.8	0.003
22	<i>Fermt1</i>	5.8	0.036
23	<i>Fgd4</i>	37.1	0.009
24	<i>Fgf9</i>	57.2	0.022
25	<i>Fgfbp1</i>	1831.0	0.002
26	<i>Fgfr1</i>	3.0	0.007
27	<i>Fhl2</i>	-2.3	0.015
28	<i>Fhod1</i>	4.1	0.006
29	<i>Fibp</i>	1.5	0.005
30	<i>Flrt1</i>	123.3	0.010
31	<i>Flrt3</i>	-3.5	0.025
32	<i>Flt3</i>	27.8	0.023
33	<i>Fmr1</i>	2.1	0.006
34	<i>Fndc3a</i>	3.3	0.002
35	<i>Fnip1</i>	2.7	0.008
36	<i>Fnip2</i>	23.1	0.007
37	<i>Folh1</i>	-151.6	0.044
38	<i>Folr2</i>	3.5	0.010
39	<i>Foxi3</i>	45.4	0.037
40	<i>Foxj1</i>	109.3	0.021
41	<i>Foxk1</i>	-3.7	0.040
42	<i>Foxo3</i>	2.2	0.015
43	<i>Foxo4</i>	6.1	0.024
44	<i>Fpr1</i>	-282.3	0.003
45	<i>Frmd3</i>	-143.3	0.027
46	<i>Fscn3</i>	531.0	0.006
47	<i>Fsd1</i>	-242.3	0.011
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<i>Fto</i>	-5.3	0.004
<i>Fundc2</i>	1.6	0.015
<i>Furin</i>	-2.0	0.000
<i>Fut11</i>	-2.8	0.037
<i>Fut7</i>	215.2	0.003
<i>Fut8</i>	-5.7	0.000
<i>Fxyd1</i>	1.8	0.038
<i>Fxyd2</i>	6.8	0.000
<i>Fxyd3</i>	5.4	0.034
<i>G3bp1</i>	-1.9	0.002
<i>G3bp2</i>	-4.0	0.024
<i>Gabarapl1</i>	1.8	0.003
<i>Gabbr1</i>	2.9	0.007
<i>Gabbr2</i>	533.6	0.004
<i>Gabrd</i>	39.1	0.019
<i>Gadd45g</i>	1.8	0.021
<i>Gale</i>	2.5	0.017
<i>Galm</i>	2.2	0.037
<i>Galnt1</i>	-3.2	0.009
<i>Galnt10</i>	-4.4	0.002
<i>Galt</i>	1.6	0.050
<i>Gatad2b</i>	2.9	0.019
<i>Gatm</i>	-2.7	0.009
<i>Gba2</i>	1.8	0.034
<i>Gc</i>	-122.8	0.017
<i>Gcgr</i>	27.5	0.025
<i>Gcn1l1</i>	1.8	0.040
<i>Gfi1</i>	-52.5	0.017
<i>Ggps1</i>	-2.7	0.014
<i>Ghr</i>	-2.0	0.005
<i>Ghrl</i>	19.6	0.042
<i>Gimap4</i>	2.6	0.024
<i>Gimap7</i>	-12.6	0.028
<i>Gjb2</i>	43.7	0.022
<i>Gjb3</i>	131.2	0.027
<i>Gjc1</i>	-2.6	0.004
<i>Gldn</i>	23.6	0.035
<i>Glrb</i>	-70.6	0.008
<i>Glrx</i>	-2.4	0.001
<i>Gls</i>	1.8	0.018
<i>Gls</i>	1.8	0.018
<i>Gmnn</i>	-2.6	0.009
<i>Gmppa</i>	1.8	0.006
<i>Gmppb</i>	-2.8	0.000
<i>Gmps</i>	-1.7	0.029
<i>Gnai3</i>	-1.5	0.012

<i>Gnal</i>	-1.7	0.018
<i>Gnb1</i>	-1.6	0.014
<i>Gngt2</i>	2.3	0.013
<i>Gnl2</i>	-2.5	0.005
<i>Gnl3</i>	-1.5	0.019
<i>Gnpda2</i>	-2.9	0.028
<i>Gnpnat1</i>	-2.2	0.003
<i>Golga1</i>	3.8	0.003
<i>Golga7</i>	-1.9	0.026
<i>Golt1b</i>	-1.7	0.040
<i>Gorasp2</i>	-1.5	0.043
<i>Gpc1</i>	1.7	0.030
<i>Gpc3</i>	-10.5	0.000
<i>Gpc4</i>	-1.7	0.043
<i>Gpcpd1</i>	-2.6	0.002
<i>Gpnmb</i>	3.1	0.033
<i>Gpr174</i>	58.6	0.010
<i>Gprc5a</i>	65.2	0.021
<i>Gpsm2</i>	-2.5	0.001
<i>Grb10</i>	-1.8	0.029
<i>Grik4</i>	108.0	0.005
<i>Grin2c</i>	-84.4	0.049
<i>Grm7</i>	64.4	0.029
<i>Grsf1</i>	-1.8	0.001
<i>Gsn</i>	2.1	0.001
<i>Gsr</i>	-2.1	0.014
<i>Gstk1</i>	2.2	0.020
<i>Gstm5</i>	-1.8	0.012
<i>Gtpbp2</i>	3.1	0.000
<i>Haao</i>	-139.1	0.014
<i>Hadh</i>	-2.5	0.044
<i>Hat1</i>	-2.6	0.000
<i>Havcr2</i>	-327.5	0.027
<i>Hbp1</i>	-2.1	0.002
<i>Hcfc1r1</i>	1.7	0.017
<i>Hdac1</i>	-1.6	0.018
<i>Hdac10</i>	2.5	0.036
<i>Hdac2</i>	-1.8	0.000
<i>Hexa</i>	1.7	0.005
<i>Hexim2</i>	-2.2	0.016
<i>Hgfac</i>	265.0	0.011
<i>Hibadh</i>	-2.2	0.013
<i>Hif1a</i>	-1.9	0.002
<i>Higd1a</i>	1.6	0.031
<i>Hint2</i>	2.1	0.007
<i>Hip1</i>	2.0	0.014



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2	<i>Hipk2</i>	3.7	0.031
3	<i>Hist1h2bh</i>	2.1	0.012
4	<i>Hist1h4m,Hist1h4b</i>	#N/A	#N/A
5	<i>Hivep1</i>	3.1	0.019
6	<i>Hivep3</i>	-4.9	0.028
7	<i>Hmgcl</i>	2.1	0.010
8	<i>Hmgn2</i>	-2.3	0.000
9	<i>Hnrnpa2b1</i>	-1.8	0.017
10	<i>Hnrnpdl</i>	-1.6	0.020
11	<i>Hnrnpf</i>	-1.8	0.030
12	<i>Hnrnp2</i>	-2.2	0.033
13	<i>Hnrnpu</i>	-1.5	0.002
14	<i>Hoxb4</i>	-27.5	0.042
15	<i>Hoxd4</i>	6.8	0.031
16	<i>Hoxd9</i>	31.9	0.044
17	<i>Hp</i>	-3.3	0.036
18	<i>Hpd</i>	-110.3	0.027
19	<i>Hras</i>	1.6	0.027
20	<i>Hrh1</i>	-260.9	0.025
21	<i>Hrh3</i>	-311.0	0.011
22	<i>Hrk</i>	66.4	0.032
23	<i>Hsd17b14</i>	97.6	0.023
24	<i>Hsd17b8</i>	2.4	0.001
25	<i>Hsdl2</i>	-1.9	0.045
26	<i>Hsf2</i>	-2.2	0.028
27	<i>Hspa1l</i>	128.5	0.022
28	<i>Hspa5</i>	-1.7	0.002
29	<i>Hspb1</i>	4.6	0.000
30	<i>Hsph1</i>	2.1	0.013
31	<i>Htr1b</i>	-87.1	0.027
32	<i>Htr2b</i>	50.1	0.015
33	<i>Htr7</i>	-107.7	0.027
34	<i>Ica1</i>	2.9	0.024
35	<i>Icam4</i>	-322.7	0.009
36	<i>Icam5</i>	30.9	0.034
37	<i>Idh3a</i>	-1.9	0.012
38	<i>Ifi27</i>	1.9	0.013
39	<i>Ifi27l2b</i>	7.6	0.000
40	<i>Ifngr2</i>	1.7	0.014
41	<i>Ift57</i>	-1.8	0.004
42	<i>Igbp1</i>	1.9	0.030
43	<i>Igfbp6</i>	54.1	0.000
44	<i>Ikbip</i>	-2.7	0.002
45	<i>Il11</i>	83.2	0.026
46	<i>Il16</i>	-10.1	0.000
47	<i>Il1rl1</i>	-27.1	0.021
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2	<i>Il3ra</i>	2.5	0.020
3	<i>Ilf2</i>	-1.8	0.017
4	<i>Ilf3</i>	1.6	0.033
5	<i>Impa1</i>	-2.2	0.001
6	<i>Ina</i>	-32.5	0.035
7	<i>Ing4</i>	1.6	0.007
8	<i>Inha</i>	6.7	0.009
9	<i>Inhba</i>	3.1	0.026
10	<i>Ino80</i>	2.5	0.039
11	<i>Insc</i>	-2.0	0.030
12	<i>Insig2</i>	1.9	0.029
13	<i>Insl3</i>	143.6	0.017
14	<i>Ip6k1</i>	-2.8	0.015
15	<i>Ireb2</i>	-2.6	0.041
16	<i>Irf3</i>	1.9	0.011
17	<i>Irgm</i>	4.3	0.012
18	<i>Irx2</i>	51.0	0.008
19	<i>Irx6</i>	198.9	0.005
20	<i>Isoc1</i>	-2.5	0.001
21	<i>Itch</i>	-3.9	0.027
22	<i>Itga10</i>	5.5	0.001
23	<i>Itga11</i>	-2.9	0.009
24	<i>Itga4</i>	-9.7	0.005
25	<i>Itga8</i>	28.9	0.021
26	<i>Itgae</i>	1.8	0.039
27	<i>Itgb1bp2</i>	66.9	0.017
28	<i>Itgb4</i>	3.1	0.009
29	<i>Itgb6</i>	142.4	0.013
30	<i>Itm2a</i>	-2.4	0.002
31	<i>Itpka</i>	300.2	0.010
32	<i>Itpkb</i>	-8.6	0.023
33	<i>Itsn1</i>	-3.2	0.020
34	<i>Jade3</i>	-536.5	0.002
35	<i>Jmjd1c</i>	1.9	0.011
36	<i>Jmjd8</i>	1.7	0.006
37	<i>Junb</i>	1.9	0.010
38	<i>Kank1</i>	3.9	0.017
39	<i>Kars</i>	-1.6	0.007
40	<i>Kat7</i>	-1.8	0.049
41	<i>Kcna1</i>	149.8	0.018
42	<i>Kcna2</i>	-182.6	0.045
43	<i>Kcna3</i>	-92.5	0.043
44	<i>Kcnab3</i>	108.8	0.007
45	<i>Kcng1</i>	-338.6	0.005
46	<i>Kcnj12</i>	122.8	0.039
47	<i>Kcnj15</i>	93.7	0.021
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2	<i>Kcnj9</i>	86.0	0.016
3	<i>Kcnmb4</i>	3.1	0.001
4	<i>Kcnq1</i>	126.4	0.021
5	<i>Kcnrg</i>	-178.6	0.005
6	<i>Kctd1</i>	1.9	0.033
7	<i>Kctd3</i>	-3.3	0.001
8	<i>Kdelc2</i>	-1.7	0.049
9	<i>Kdm1a</i>	-1.7	0.003
10	<i>Kdm4c</i>	-11.3	0.000
11	<i>Kdm8</i>	2.0	0.038
12	<i>Keap1</i>	1.8	0.007
13	<i>Kif19</i>	72.2	0.037
14	<i>Kif1c</i>	2.7	0.030
15	<i>Kif26b</i>	-4.6	0.030
16	<i>Kif27</i>	-91.5	0.016
17	<i>Kifc2</i>	15.4	0.039
18	<i>Kit</i>	-33.8	0.013
19	<i>Klf1</i>	-30.1	0.002
20	<i>Klf13</i>	1.9	0.004
21	<i>Klf16</i>	-2.1	0.004
22	<i>Klf3</i>	1.7	0.007
23	<i>Klf4</i>	6.5	0.000
24	<i>Klf5</i>	4.5	0.026
25	<i>Klhdc10</i>	-3.3	0.040
26	<i>Klhdc3</i>	-1.8	0.001
27	<i>Klhl14</i>	-25.3	0.037
28	<i>Klhl22</i>	-1.6	0.034
29	<i>Klhl40</i>	209.8	0.026
30	<i>Klhl41</i>	145.5	0.015
31	<i>Klhl8</i>	2.1	0.034
32	<i>Klhl9</i>	-1.7	0.011
33	<i>Klk4</i>	-2388.5	0.004
34	<i>Klk8</i>	115.4	0.021
35	<i>Klk8</i>	115.4	0.021
36	<i>Klrk1</i>	-114.8	0.025
37	<i>Kmt2e</i>	1.8	0.002
38	<i>Kpna1</i>	-2.5	0.047
39	<i>Kpnb1</i>	-2.4	0.010
40	<i>Krt10</i>	2.4	0.034
41	<i>Krt15</i>	366.7	0.013
42	<i>Krt17</i>	21.1	0.033
43	<i>Krt80</i>	611.8	0.008
44	<i>Ksr1</i>	-6.0	0.011
45	<i>L3mbtl2</i>	2.0	0.035
46	<i>Lamtor2</i>	1.7	0.011
47	<i>Lamtor4</i>	1.7	0.009
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2	<i>Lancl2</i>	-4.1	0.036
3	<i>Laptm4b</i>	-2.0	0.000
4	<i>Larp6</i>	3.8	0.002
5	<i>Lbr</i>	-3.2	0.032
6	<i>Lbr</i>	-3.2	0.032
7	<i>Ldah</i>	-3.1	0.003
8	<i>Ldb2</i>	2.5	0.010
9	<i>Leprot</i>	1.7	0.004
10	<i>Lgals3</i>	5.3	0.000
11	<i>Lgals7</i>	165.8	0.002
12	<i>Lgr5</i>	390.4	0.014
13	<i>Lime1</i>	13.5	0.004
14	<i>Lims1</i>	-2.3	0.001
15	<i>Liph</i>	105.6	0.024
16	<i>Litaf</i>	1.8	0.003
17	<i>Lix1l</i>	2.2	0.006
18	<i>Llg1</i>	-2.0	0.003
19	<i>Lmbr1l</i>	2.7	0.041
20	<i>Lmf2</i>	2.0	0.000
21	<i>Lmna</i>	1.5	0.033
22	<i>Lmnb1</i>	-3.1	0.017
23	<i>LOC100302465</i>	-164.2	0.023
24	<i>Lpar6</i>	-1.7	0.050
25	<i>Lpp</i>	2.3	0.030
26	<i>Lrfn4</i>	1.8	0.030
27	<i>Lrrc1</i>	-4.4	0.044
28	<i>Lrrc29</i>	255.4	0.001
29	<i>Lrrc46</i>	802.5	0.001
30	<i>Lrrc4b</i>	2.6	0.031
31	<i>Lrrc59</i>	-1.6	0.048
32	<i>Lrrn3</i>	-19.7	0.036
33	<i>LRRTM1</i>	-28.4	0.007
34	<i>Lsm14a</i>	-1.5	0.031
35	<i>Lsm8</i>	1.6	0.025
36	<i>Lss</i>	-10.1	0.001
37	<i>Lst1</i>	-5.0	0.010
38	<i>Lta4h</i>	-1.8	0.030
39	<i>Ltbp1</i>	2.8	0.001
40	<i>Ltv1</i>	-1.9	0.012
41	<i>Luc7l</i>	2.2	0.001
42	<i>Ly6d</i>	840.4	0.000
43	<i>Ly6g6f</i>	-78.6	0.028
44	<i>Lynx1</i>	835.0	0.020
45	<i>Lypd3</i>	12.4	0.022
46	<i>Lypla1</i>	-2.1	0.003
47	<i>Magt1</i>	-3.6	0.000
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<i>Mal2</i>	113.9	0.010
<i>Mamdc4</i>	73.4	0.016
<i>Man1a1</i>	-3.6	0.027
<i>Maoa</i>	-2.4	0.033
<i>Map2</i>	-25.9	0.033
<i>Map2</i>	-25.9	0.033
<i>Map3k11</i>	2.1	0.040
<i>Map4k1</i>	-3.2	0.012
<i>Map4k4</i>	2.4	0.022
<i>Mapk11</i>	139.4	0.017
<i>Mapk13</i>	64.3	0.007
<i>Mapre1</i>	-1.6	0.009
<i>Mapt</i>	20.7	0.042
<i>Marc1</i>	4.3	0.036
<i>March2</i>	2.3	0.000
<i>March3</i>	-4.1	0.015
<i>March5</i>	-2.2	0.010
<i>March7</i>	-7.2	0.000
<i>Matk</i>	4.5	0.026
<i>Mbip</i>	-2.5	0.020
<i>Mcc</i>	21.3	0.027
<i>Mccc1</i>	-2.5	0.049
<i>Mccc2</i>	-1.9	0.048
<i>Mcfd2</i>	-1.9	0.001
<i>Mcl1</i>	-1.6	0.026
<i>Mcm10</i>	-43.8	0.000
<i>Mcm2</i>	-2.8	0.005
<i>Mcm4</i>	-2.1	0.010
<i>Mcm6</i>	-2.6	0.017
<i>Mcoln3</i>	75.4	0.014
<i>Mcpt2</i>	-421.7	0.003
<i>Mdfic</i>	1.7	0.043
<i>Mdk</i>	-1.7	0.031
<i>Me3</i>	131.8	0.003
<i>Mea1</i>	1.6	0.014
<i>Med13</i>	2.3	0.006
<i>Med15</i>	1.7	0.003
<i>Med19</i>	1.7	0.029
<i>Med20</i>	-2.0	0.009
<i>Med31</i>	1.8	0.002
<i>Mef2b</i>	-53.1	0.047
<i>Mei4</i>	-137.5	0.028
<i>Mest</i>	-6.6	0.000
<i>Mettl23</i>	1.8	0.030
<i>Mettl4</i>	-12.7	0.025
<i>Mfsd12</i>	-26.6	0.014

<i>Mgarp</i>	341.5	0.005
<i>Mgp</i>	2.2	0.034
<i>Mgrn1</i>	-2.8	0.006
<i>Mid1ip1</i>	2.3	0.023
<i>Mina</i>	-3.0	0.001
<i>Mios</i>	-2.9	0.001
<i>Mis12</i>	-2.5	0.022
<i>Mknk2</i>	-1.6	0.020
<i>Mlana</i>	35.3	0.001
<i>MIph</i>	76.0	0.020
<i>Mmgt1</i>	-2.8	0.049
<i>Mmp23</i>	-1.8	0.038
<i>Mmp24</i>	2.2	0.019
<i>Mmp3</i>	107.3	0.012
<i>Mok</i>	4.7	0.036
<i>Morc1</i>	-58.8	0.038
<i>Morf4l2</i>	-1.7	0.001
<i>Mospd4</i>	146.2	0.013
<i>Mpc2</i>	1.9	0.008
<i>Mpg</i>	1.6	0.040
<i>Mpp6</i>	-1.9	0.015
<i>Mprip</i>	-1.5	0.015
<i>Mpv17l2</i>	1.7	0.022
<i>Mpzl2</i>	21.1	0.023
<i>Mrc1</i>	1.8	0.031
<i>Mri1</i>	2.8	0.004
<i>Mrpl14</i>	1.6	0.022
<i>Mrpl32</i>	1.7	0.009
<i>Mrpl54</i>	1.8	0.041
<i>mrpl9</i>	2.1	0.001
<i>Mrps2</i>	-2.0	0.026
<i>Mrps22</i>	1.8	0.049
<i>Mrps27</i>	-2.2	0.049
<i>Mrps30</i>	-1.8	0.025
<i>Ms4a1</i>	-12.6	0.014
<i>Ms4a2</i>	-40.1	0.014
<i>Msl1</i>	1.7	0.006
<i>Mst1r</i>	41.7	0.049
<i>Msto1</i>	2.2	0.047
<i>Mt1a</i>	7.5	0.000
<i>Mt3</i>	60.7	0.000
<i>Mt4</i>	1334.1	0.003
<i>Mta2</i>	-1.7	0.015
<i>Mterfd1</i>	-2.2	0.000
<i>Mtf2</i>	-1.6	0.041
<i>Mtmr2</i>	-1.8	0.048

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2	<i>Mtmr7</i>	-52.9	0.020
3	<i>Mto1</i>	3.2	0.037
4	<i>Mtrr</i>	2.7	0.017
5	<i>Muc1</i>	233.8	0.004
6	<i>Muc20</i>	-445.1	0.007
7	<i>Mvb12a</i>	1.9	0.002
8	<i>Mx2</i>	229.4	0.010
9	<i>Mybl1</i>	80.7	0.010
10	<i>Myc</i>	-2.0	0.001
11	<i>Mycbp2</i>	2.1	0.028
12	<i>Myh10</i>	-1.6	0.043
13	<i>Myl1</i>	1233.0	0.003
14	<i>Mylpf</i>	6.6	0.043
15	<i>Myo1d</i>	3.0	0.001
16	<i>Myo1e</i>	2.6	0.043
17	<i>Myo7a</i>	30.1	0.045
18	<i>Myo9a</i>	3.3	0.006
19	<i>Myoc</i>	155.0	0.011
20	<i>Myof</i>	2.5	0.019
21	<i>Myom2</i>	706.7	0.004
22	<i>Mzb1</i>	-17.6	0.021
23	<i>N4bp2l2</i>	1.7	0.008
24	<i>Nadk2</i>	-3.7	0.010
25	<i>Nags</i>	82.2	0.006
26	<i>Ncaph2</i>	-2.0	0.012
27	<i>Ncbp1</i>	-1.9	0.003
28	<i>Ncf2</i>	-117.9	0.014
29	<i>Ncoa5</i>	-2.6	0.000
30	<i>Ndel1</i>	-1.6	0.033
31	<i>Ndfip2</i>	-1.9	0.004
32	<i>Ndufa10</i>	-1.7	0.004
33	<i>Ndufaf1</i>	-9.7	0.006
34	<i>Ndufs5</i>	2.3	0.003
35	<i>Nek6</i>	-4.0	0.000
36	<i>Neto2</i>	-5.7	0.046
37	<i>Neu3</i>	25.5	0.012
38	<i>Nfat5</i>	2.1	0.047
39	<i>Nfatc1</i>	1.7	0.017
40	<i>Nfil3</i>	-2.3	0.019
41	<i>Nfkbia</i>	1.5	0.002
42	<i>Nfkbiz</i>	6.4	0.011
43	<i>Nfx1</i>	-2.6	0.001
44	<i>Ngp</i>	-19.0	0.011
45	<i>Nin</i>	6.7	0.003
46	<i>Nkx2-3</i>	67.5	0.028
47	<i>Nkx6-3</i>	94.9	0.009
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<i>Nmbr</i>	49.8	0.044
<i>Nmnat2</i>	70.0	0.026
<i>Nmur1</i>	-108.6	0.030
<i>Nnat</i>	4.5	0.000
<i>Nnt</i>	-1.5	0.017
<i>Nob1</i>	1.7	0.011
<i>Noc2l</i>	-3.1	0.001
<i>Nod2</i>	23.3	0.037
<i>Nol10</i>	-2.4	0.019
<i>Nop56</i>	-1.7	0.033
<i>Nop58</i>	-1.5	0.028
<i>Nos1</i>	41.0	0.035
<i>Nos2</i>	63.9	0.025
<i>Notch1</i>	2.1	0.011
<i>Notch4</i>	2.1	0.018
<i>Npas2</i>	5.5	0.010
<i>Npc1</i>	3.0	0.003
<i>Nphs1</i>	67.9	0.027
<i>Npr3</i>	-423.3	0.014
<i>Nptn</i>	1.6	0.005
<i>Npy4r</i>	-131.4	0.035
<i>Npy5r</i>	64.0	0.040
<i>Nr0b2</i>	416.4	0.002
<i>Nr1h2</i>	1.7	0.002
<i>Nr2c1</i>	-2.3	0.017
<i>Nr4a1</i>	2.4	0.047
<i>Nras</i>	-2.2	0.047
<i>Nrg1</i>	103.2	0.011
<i>Nrg1</i>	103.2	0.011
<i>Nrg2</i>	-8.5	0.043
<i>Nrp2</i>	-2.2	0.042
<i>Nrxn1</i>	-5.6	0.039
<i>Nsg1</i>	-1.9	0.022
<i>Nsmce4a</i>	-1.7	0.014
<i>Nsun2</i>	-2.3	0.001
<i>Nt5c1b</i>	-70.8	0.048
<i>Ntmt1</i>	1.6	0.005
<i>Ntn3</i>	-3.0	0.048
<i>Nuak2</i>	14.4	0.027
<i>Nudt17</i>	342.1	0.005
<i>Nufip1</i>	-2.1	0.013
<i>Numa1</i>	2.0	0.003
<i>Nup35</i>	-1.8	0.034
<i>Nup62</i>	-2.1	0.003
<i>Nup93</i>	-1.9	0.012
<i>Nupl1</i>	-5.9	0.004



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<i>Nus1</i>	-1.8	0.010
<i>Oas3</i>	81.3	0.017
<i>Oat</i>	-1.6	0.001
<i>Ogdhl</i>	13.2	0.014
<i>Ogdhl,Ogdh</i>	#N/A	#N/A
<i>Ogfr</i>	1.7	0.004
<i>Olfr4</i>	-16.4	0.045
<i>Ormdl2</i>	2.1	0.001
<i>Ormdl3</i>	-1.9	0.044
<i>Ovol1</i>	120.7	0.009
<i>P2rx3</i>	-14.2	0.038
<i>P2ry2</i>	2.8	0.047
<i>P4ha3</i>	-3.4	0.004
<i>Pafah1b2</i>	-3.0	0.000
<i>Pafah2</i>	-104.0	0.004
<i>Pak1</i>	-3.7	0.001
<i>Pak3</i>	-4.6	0.039
<i>Palmd</i>	3.5	0.006
<i>Palmd</i>	3.5	0.006
<i>Pam16</i>	1.9	0.024
<i>Pam16</i>	1.9	0.024
<i>Pard3b</i>	2.4	0.024
<i>Pard6g</i>	-2.8	0.000
<i>Parl</i>	-1.6	0.015
<i>Parvg</i>	-41.7	0.009
<i>Pax8</i>	724.6	0.001
<i>Paxip1</i>	-2.0	0.039
<i>Pc</i>	-2.9	0.018
<i>Pc</i>	-2.9	0.018
<i>Pccb</i>	-1.8	0.006
<i>Pcdh18</i>	-2.2	0.033
<i>Pcdh9</i>	-11.9	0.001
<i>Pcdhga8</i>	55.3	0.029
<i>Pck2</i>	1.9	0.005
<i>Pcmt1</i>	1.6	0.025
<i>Pcmt2</i>	1.6	0.044
<i>Pcsk1</i>	1275.4	0.000
<i>Pcsk1</i>	1275.4	0.000
<i>Pde10a</i>	411.1	0.001
<i>Pde1b</i>	-291.6	0.018
<i>Pde4dip</i>	-2.1	0.006
<i>Pdia4</i>	-1.9	0.001
<i>Pdia6</i>	-2.2	0.000
<i>Pdk1</i>	-1.8	0.015
<i>Pdk1</i>	-1.8	0.015
<i>Pdlim2</i>	2.2	0.012

<i>Pdlim5</i>	-3.2	0.002
<i>Pdpr</i>	-235.7	0.002
<i>Pdxp</i>	-3.2	0.000
<i>Pdzd2</i>	4.2	0.014
<i>Pdzd7</i>	175.7	0.025
<i>Pecam1</i>	1.9	0.014
<i>Peg3</i>	-2.0	0.029
<i>Peg3</i>	-2.0	0.029
<i>Peli1</i>	-2.4	0.027
<i>Penk</i>	-2.4	0.020
<i>Per3</i>	-3.8	0.034
<i>Pet100</i>	1.6	0.037
<i>Pex11b</i>	-2.5	0.028
<i>Pex13</i>	-1.7	0.022
<i>Pex16</i>	2.3	0.001
<i>Pex26</i>	4.3	0.005
<i>Pex6</i>	2.0	0.042
<i>Pex7</i>	-8.9	0.001
<i>Pfdn6</i>	2.0	0.049
<i>Pgam2</i>	-21.0	0.036
<i>Pgbd5</i>	-410.6	0.008
<i>Pggt1b</i>	-3.7	0.014
<i>Pgp</i>	1.5	0.023
<i>Phb2</i>	-1.5	0.005
<i>Phkg1</i>	134.3	0.016
<i>Phkg2</i>	1.9	0.004
<i>Pias2</i>	-1.8	0.040
<i>Picalm</i>	-2.1	0.030
<i>Pid1</i>	-3.4	0.013
<i>Pigl</i>	6.8	0.002
<i>Pigm</i>	-6.7	0.016
<i>Pign</i>	-10.2	0.023
<i>Pigp</i>	2.8	0.000
<i>Pih1d2</i>	3.2	0.019
<i>Pik3c2a</i>	2.9	0.008
<i>Pik3c2g</i>	33.6	0.042
<i>Pik3cb</i>	27.4	0.011
<i>Pik3r1</i>	4.1	0.006
<i>Pim3</i>	2.5	0.000
<i>Pirt</i>	-175.4	0.015
<i>Pkd1</i>	2.0	0.015
<i>Pkdcc</i>	-2.0	0.006
<i>Pkig</i>	1.7	0.014
<i>Pknox2</i>	-19.6	0.023
<i>Pla2g12a</i>	2.6	0.027
<i>Pla2g5</i>	7.9	0.000

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<i>Pla2g7</i>	4.0	0.046
<i>Plag1</i>	198.1	0.009
<i>Plcb2</i>	115.8	0.001
<i>Plcg1</i>	1.8	0.037
<i>Plec</i>	1.8	0.017
<i>Plekha3</i>	-1.5	0.036
<i>Plekha4</i>	6.0	0.034
<i>Plekha8</i>	2.4	0.045
<i>Plekhf1</i>	1.9	0.006
<i>Plekhn1</i>	867.1	0.001
<i>Plet1</i>	549.9	0.017
<i>Plg</i>	411.9	0.006
<i>Plin1</i>	80.0	0.021
<i>Plod3</i>	1.6	0.042
<i>Pnlsr</i>	2.3	0.003
<i>Pnpla7</i>	4.0	0.000
<i>Pof1b</i>	216.9	0.003
<i>Pold4</i>	1.6	0.026
<i>Poli</i>	21.1	0.020
<i>Polr1a,Rpa1</i>	#N/A	#N/A
<i>Polr2k</i>	2.5	0.004
<i>Polr2m</i>	-1.9	0.015
<i>Polr3e</i>	-2.6	0.002
<i>Pon2</i>	-2.0	0.005
<i>Pop5</i>	2.3	0.001
<i>Popdc3</i>	-332.3	0.012
<i>Porcn</i>	1.9	0.024
<i>Pot1</i>	-2.8	0.013
<i>Pou2af1</i>	-21.5	0.030
<i>Pou3f3</i>	39.6	0.035
<i>Ppa2</i>	-2.0	0.004
<i>Ppef2</i>	54.9	0.024
<i>Ppfia3</i>	-63.7	0.003
<i>Ppfibp2</i>	2.3	0.002
<i>Ppm1a</i>	-1.7	0.013
<i>Ppm1g</i>	-1.6	0.007
<i>Ppp1r10</i>	1.5	0.040
<i>Ppp1r14b</i>	1.6	0.032
<i>Ppp1r7</i>	-1.7	0.034
<i>Ppp1r8</i>	2.2	0.013
<i>Ppp1r9a</i>	52.8	0.044
<i>Ppp2ca</i>	-1.6	0.039
<i>Ppp2r1b</i>	-2.6	0.024
<i>Ppp2r5c</i>	-1.7	0.011
<i>Ppp3cc</i>	-2.4	0.003
<i>Ppp3r1</i>	-2.3	0.002

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2	<i>Prdm2</i>	2.4	0.048
3	<i>Prdx3</i>	-1.6	0.015
4	<i>Prickle2</i>	-2.3	0.032
5	<i>Prkar1a</i>	-1.8	0.002
6	<i>Prkcd</i>	-2.4	0.001
7	<i>Prkcq</i>	-26.1	0.034
8	<i>Prkcsh</i>	1.6	0.003
9	<i>Prkx</i>	-3.5	0.007
10	<i>Prmt3</i>	-3.0	0.003
11	<i>Proc</i>	124.7	0.029
12	<i>Prokr2</i>	-167.6	0.000
13	<i>Prox2</i>	94.0	0.031
14	<i>Prpf18</i>	2.0	0.017
15	<i>Prpf38b</i>	1.6	0.033
16	<i>Prpf40a</i>	-1.5	0.005
17	<i>Prpf40b</i>	2.0	0.042
18	<i>Prps1</i>	-2.2	0.006
19	<i>Prr13</i>	1.8	0.005
20	<i>Prss12</i>	-5.3	0.000
21	<i>Prss30</i>	-129.5	0.037
22	<i>Prss8</i>	301.4	0.003
23	<i>Psat1</i>	-4.1	0.017
24	<i>Psemb10</i>	1.7	0.028
25	<i>Psmc3</i>	-1.6	0.016
26	<i>Pstpip1</i>	4.7	0.010
27	<i>Pstpip2</i>	-18.3	0.025
28	<i>Ptbp2</i>	-4.3	0.024
29	<i>Ptch2</i>	29.1	0.050
30	<i>Ptdss1</i>	-1.9	0.001
31	<i>Ptdss2</i>	-2.0	0.003
32	<i>Ptger2</i>	113.7	0.012
33	<i>Ptges</i>	-2.5	0.006
34	<i>Ptges3l1</i>	-12.4	0.008
35	<i>Ptgis</i>	4.1	0.000
36	<i>Ptgs1</i>	-3.8	0.008
37	<i>Ptgs2</i>	-225.2	0.012
38	<i>Ptk2</i>	-1.6	0.009
39	<i>Ptk7</i>	-1.5	0.046
40	<i>Ptp4a1</i>	-2.9	0.023
41	<i>Ptpn12</i>	2.1	0.018
42	<i>Ptpn2</i>	-1.8	0.027
43	<i>Ptpre</i>	3.2	0.004
44	<i>Ptprn</i>	183.4	0.013
45	<i>Ptprz1</i>	2.3	0.017
46	<i>Purb</i>	1.5	0.046
47	<i>Pvalb</i>	33.6	0.042
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2	<i>Pwp2</i>	-2.8	0.029
3	<i>Pycr2</i>	1.6	0.004
4	<i>Pycrl</i>	-1.6	0.034
5	<i>Qdpr</i>	-1.7	0.039
6	<i>Rab18</i>	-1.6	0.024
7	<i>Rab1b</i>	-2.3	0.027
8	<i>Rab31</i>	1.6	0.033
9	<i>Rab39a</i>	63.9	0.021
10	<i>Rab3b</i>	123.6	0.023
11	<i>Rab5a</i>	-3.0	0.022
12	<i>Rab6b</i>	-5.4	0.045
13	<i>Rab8a</i>	-1.6	0.000
14	<i>Rabgap1l</i>	3.5	0.037
15	<i>Rabggta</i>	-2.0	0.029
16	<i>Rabggtb</i>	1.8	0.048
17	<i>Racgap1</i>	-6.0	0.004
18	<i>Rag1</i>	-28.2	0.044
19	<i>Rag2</i>	-559.7	0.006
20	<i>Ralbp1</i>	1.8	0.026
21	<i>Raly</i>	-1.6	0.002
22	<i>Ramp1</i>	2.3	0.000
23	<i>Rap1b</i>	-2.0	0.031
24	<i>Rapgef6</i>	-3.3	0.025
25	<i>Rarb</i>	-6.7	0.006
26	<i>Rasa1</i>	681.4	0.002
27	<i>Raver1</i>	-1.8	0.008
28	<i>Rbbp7</i>	-1.9	0.002
29	<i>Rbbp9</i>	-2.4	0.023
30	<i>Rbp2</i>	106.2	0.035
31	<i>Rbp2</i>	106.2	0.035
32	<i>Rbsn</i>	-2.1	0.036
33	<i>Rcbtb1</i>	-2.9	0.020
34	<i>Rcl1</i>	-2.0	0.038
35	<i>Rcl1,Clns1a</i>	#N/A	#N/A
36	<i>Rcor1</i>	1.7	0.011
37	<i>Rdh12</i>	227.6	0.003
38	<i>Rdm1</i>	1.9	0.042
39	<i>Reep2</i>	46.7	0.012
40	<i>Reep4</i>	2.0	0.025
41	<i>Reep5</i>	1.5	0.006
42	<i>Reln</i>	-14.2	0.048
43	<i>Rem2</i>	33.0	0.040
44	<i>Rev1</i>	-2.0	0.012
45	<i>Rfwd2</i>	-1.8	0.001
46	<i>Rfx6</i>	39.6	0.039
47	<i>RGD1309730</i>	1.8	0.023

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2	<i>RGD1311892</i>	64.8	0.030
3	<i>RGD1560436</i>	-96.7	0.031
4	<i>RGD1561102</i>	-168.7	0.025
5	<i>RGD1564379</i>	-1.6	0.009
6	<i>Rgs10</i>	2.0	0.009
7	<i>Rgs18</i>	-43.7	0.000
8	<i>Rgs2</i>	-2.5	0.010
9	<i>Rgs3</i>	2.0	0.003
10	<i>Rgs7</i>	-146.2	0.041
11	<i>Rhd</i>	-19.7	0.005
12	<i>Rhoh</i>	-7.6	0.025
13	<i>Rhot2</i>	2.7	0.006
14	<i>Rims2</i>	-197.4	0.003
15	<i>Ring1</i>	1.6	0.022
16	<i>Riok2</i>	-1.9	0.039
17	<i>Rita1</i>	2.6	0.003
18	<i>Rnaseh1</i>	2.0	0.040
19	<i>Rnaseh2a</i>	2.2	0.002
20	<i>Rnaseh2b</i>	-2.0	0.010
21	<i>Rnf111</i>	1.8	0.040
22	<i>Rnf114</i>	-1.6	0.002
23	<i>Rnf111l</i>	-2.7	0.006
24	<i>Rnf123</i>	-2.1	0.009
25	<i>Rnf13</i>	-3.1	0.049
26	<i>Rnf2</i>	-2.0	0.002
27	<i>Rnf215</i>	1.7	0.041
28	<i>Rnf39</i>	148.1	0.010
29	<i>Rnf4</i>	-5.5	0.000
30	<i>Rnmt</i>	-1.9	0.009
31	<i>Robo1</i>	-4.2	0.023
32	<i>Rogdi</i>	-1.7	0.047
33	<i>Rpa1</i>	-7.4	0.002
34	<i>Rpa1</i>	-7.4	0.002
35	<i>Rpain</i>	2.1	0.014
36	<i>Rpf2</i>	-1.8	0.049
37	<i>Rpgrip1l</i>	3.4	0.023
38	<i>Rpl37a</i>	-16.5	0.043
39	<i>Rpn1</i>	-1.5	0.001
40	<i>Rpp21</i>	1.8	0.005
41	<i>Rpp25</i>	-64.6	0.001
42	<i>Rps17</i>	2.7	0.010
43	<i>Rps6ka3</i>	-3.8	0.000
44	<i>Rps6kb1</i>	-1.7	0.046
45	<i>Rragc</i>	-1.7	0.009
46	<i>Rras</i>	1.6	0.025
47	<i>Rreb1</i>	2.3	0.045
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<i>Rrn3</i>	-3.0	0.046
<i>Rrp8</i>	-3.7	0.010
<i>Rsad2</i>	-13.6	0.007
<i>Rs/24d1</i>	-2.0	0.009
<i>Rtkn2</i>	-33.4	0.046
<i>Rtn4rl1</i>	3.1	0.011
<i>Runx1</i>	-3.3	0.012
<i>Ruvbl2</i>	-1.7	0.023
<i>S100a10</i>	2.4	0.005
<i>S100a16</i>	1.9	0.006
<i>S100a3</i>	2.3	0.044
<i>S100a4</i>	4.3	0.007
<i>S100a6</i>	4.5	0.002
<i>Sag</i>	36.1	0.026
<i>Sag</i>	36.1	0.026
<i>Sag</i>	36.1	0.026
<i>Sat1</i>	1.7	0.008
<i>Sat1</i>	1.7	0.008
<i>Sat1</i>	1.7	0.008
<i>Saxo2</i>	331.9	0.017
<i>Sbds</i>	1.7	0.016
<i>Sbf1</i>	1.8	0.034
<i>Sbsn</i>	13.7	0.002
<i>Scap</i>	1.8	0.028
<i>Scara5</i>	11.9	0.001
<i>Scd2</i>	-2.1	0.008
<i>Scfd1</i>	-1.8	0.002
<i>Scg5</i>	331.0	0.004
<i>Scgb1a1</i>	383.4	0.005
<i>Scn2b</i>	-11.1	0.039
<i>Scube3</i>	-33.8	0.023
<i>Sdcbp</i>	-1.5	0.026
<i>Sdcbp2</i>	-144.5	0.041
<i>Sdha</i>	-2.0	0.002
<i>Sdr16c5</i>	259.0	0.013
<i>Sec13</i>	-1.7	0.002
<i>Sec14l1</i>	3.1	0.000
<i>Sec22b</i>	-2.3	0.000
<i>Sec23ip</i>	-2.1	0.003
<i>Sec24a</i>	-3.9	0.017
<i>Sec61a2</i>	-2.3	0.002
<i>Selk</i>	1.8	0.004
<i>Selt</i>	-1.6	0.002
<i>Sema3e</i>	37.2	0.032
<i>Sema4b</i>	-3.0	0.004
<i>Serp1</i>	-2.0	0.000

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2	<i>Serpinb10</i>	18.3	0.037
3	<i>Serpinb2</i>	549.6	0.001
4	<i>Serpinb8</i>	331.2	0.000
5	<i>Serpinb9</i>	-2.3	0.022
6	<i>Serpine1</i>	7.0	0.001
7	<i>Serpine2</i>	-2.1	0.022
8	<i>Sesn1</i>	-2.3	0.011
9	<i>Set</i>	-1.8	0.009
10	<i>Sf3a2</i>	-1.9	0.017
11	<i>Sf3b4</i>	-1.6	0.037
12	<i>Sfi1</i>	2.2	0.026
13	<i>Sfmbt2</i>	-147.8	0.038
14	<i>Sftpc</i>	117.9	0.019
15	<i>Sfxn1</i>	-4.0	0.003
16	<i>Sfxn3</i>	1.5	0.012
17	<i>Sgcd</i>	-2.0	0.036
18	<i>Sgpl1</i>	-6.0	0.010
19	<i>Sh2d2a</i>	-375.9	0.009
20	<i>Sh3glb2</i>	2.2	0.001
21	<i>Shc4</i>	92.0	0.022
22	<i>Shmt1</i>	-7.7	0.007
23	<i>Shpk</i>	561.9	0.000
24	<i>Shtn1</i>	14.8	0.005
25	<i>Siglec10</i>	-20.9	0.010
26	<i>Sirt3</i>	4.8	0.000
27	<i>Sirt4</i>	2.8	0.038
28	<i>Sit1</i>	-11.4	0.033
29	<i>Sit1,Slc6a20</i>	#N/A	#N/A
30	<i>Skp2</i>	-2.3	0.033
31	<i>Slamf7</i>	-169.8	0.005
32	<i>Slbp</i>	-1.6	0.042
33	<i>Slc12a4</i>	1.7	0.020
34	<i>Slc13a5</i>	3.6	0.029
35	<i>Slc15a2</i>	78.1	0.010
36	<i>Slc15a3</i>	2.6	0.020
37	<i>Slc16a1</i>	-6.2	0.001
38	<i>Slc16a13</i>	3.9	0.036
39	<i>Slc16a14</i>	45.4	0.036
40	<i>Slc16a2</i>	-5.1	0.026
41	<i>Slc1a1</i>	167.2	0.007
42	<i>Slc1a2</i>	244.6	0.008
43	<i>Slc1a3</i>	-5.5	0.000
44	<i>Slc1a6</i>	-35.1	0.014
45	<i>Slc24a4</i>	-21.9	0.032
46	<i>Slc25a23</i>	44.0	0.019
47	<i>Slc25a25</i>	-2.9	0.008
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2	<i>Slc25a28</i>	1.9	0.002
3	<i>Slc25a46</i>	-1.8	0.013
4	<i>Slc26a6</i>	4.1	0.013
5	<i>Slc28a1</i>	259.0	0.018
6	<i>Slc28a3</i>	124.1	0.009
7	<i>Slc30a10</i>	-41.1	0.038
8	<i>Slc30a3</i>	-279.3	0.012
9	<i>Slc30a6</i>	-2.3	0.014
10	<i>Slc30a7</i>	-2.0	0.021
11	<i>Slc35e4</i>	2.3	0.008
12	<i>Slc39a1</i>	3.1	0.021
13	<i>Slc39a14</i>	2.0	0.048
14	<i>Slc39a3</i>	2.7	0.000
15	<i>Slc39a8</i>	-2.4	0.008
16	<i>Slc43a2</i>	3.4	0.006
17	<i>Slc4a9</i>	320.0	0.005
18	<i>Slc52a3</i>	45.5	0.029
19	<i>Slc5a5</i>	-307.9	0.015
20	<i>Slc5a9</i>	248.0	0.027
21	<i>Slc6a8</i>	2.6	0.007
22	<i>Slc7a10</i>	-229.0	0.018
23	<i>Slc7a3</i>	60.1	0.042
24	<i>Slc8b1</i>	3.2	0.002
25	<i>Slc9a3</i>	83.1	0.011
26	<i>Slc9a8</i>	-5.8	0.011
27	<i>Slc9a9</i>	-2.7	0.025
28	<i>Slco4a1</i>	16.9	0.037
29	<i>Slit3</i>	2.5	0.002
30	<i>Slmo2</i>	-1.8	0.001
31	<i>Slx1b</i>	2.3	0.001
32	<i>Smad2</i>	-2.1	0.009
33	<i>Smad6</i>	1.9	0.044
34	<i>Smad7</i>	2.6	0.012
35	<i>Smagp</i>	2.1	0.033
36	<i>Smarcc1</i>	-2.3	0.004
37	<i>Smarcd1</i>	-1.6	0.034
38	<i>Smpd2</i>	1.9	0.028
39	<i>Snai2</i>	-2.4	0.006
40	<i>Snai3</i>	192.9	0.009
41	<i>Snca</i>	-7.8	0.031
42	<i>Snn</i>	-2.3	0.047
43	<i>Snrpd2</i>	1.6	0.042
44	<i>Snta1</i>	2.0	0.005
45	<i>Sntb1</i>	83.1	0.018
46	<i>Sntg2</i>	-216.3	0.019
47	<i>Snx6</i>	-1.7	0.000
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<i>Snx9</i>	-2.1	0.021
<i>Soat1</i>	-11.8	0.000
<i>Sox12</i>	-2.0	0.050
<i>Sp9</i>	-6.4	0.018
<i>Spib</i>	-22.8	0.001
<i>Spn</i>	9.9	0.002
<i>Spn</i>	9.9	0.002
<i>Spp1</i>	7.7	0.002
<i>Spp1</i>	7.7	0.002
<i>Spred3</i>	86.8	0.011
<i>Sprr1a</i>	2654.6	0.001
<i>Spry1</i>	2.1	0.029
<i>Spsb1</i>	-4.0	0.018
<i>Spsb4</i>	-59.9	0.007
<i>Spta1</i>	-7.7	0.043
<i>Sptbn1</i>	1.8	0.027
<i>Srd5a1</i>	-14.7	0.006
<i>Srebf2</i>	1.8	0.000
<i>Srf</i>	2.6	0.005
<i>Srp14</i>	1.6	0.002
<i>Srpk3</i>	-104.9	0.001
<i>Srprb</i>	-1.6	0.044
<i>Srrm2</i>	1.9	0.023
<i>Srsf1</i>	-1.5	0.023
<i>Srsf11</i>	1.8	0.005
<i>Srsf4</i>	-1.7	0.045
<i>Srsf5</i>	-2.3	0.000
<i>Sspo</i>	171.3	0.015
<i>Sstr2</i>	71.9	0.028
<i>St14</i>	2.7	0.033
<i>St3gal2</i>	1.9	0.004
<i>St6galnac2</i>	-2.5	0.001
<i>St8sia2</i>	-438.7	0.005
<i>Stac2</i>	-289.1	0.012
<i>Stambp</i>	-2.3	0.010
<i>Stard7</i>	-3.4	0.013
<i>Steap3</i>	1.9	0.032
<i>Stip1</i>	-1.7	0.049
<i>Stip1</i>	-1.7	0.049
<i>Stk26</i>	-17.3	0.009
<i>Stk35</i>	-3.6	0.014
<i>Stmn2</i>	69.6	0.043
<i>Strada</i>	-2.0	0.034
<i>Stt3b</i>	-3.0	0.003
<i>Stx6</i>	-1.7	0.047
<i>Stx7</i>	-2.5	0.011

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2	<i>Sulf1</i>	3.6	0.001
3	<i>Sult1a1</i>	2.7	0.047
4	<i>Sult2b1</i>	119.1	0.023
5	<i>Sumf2</i>	-1.8	0.038
6	<i>Sumo1</i>	-1.6	0.000
7	<i>Sumo2</i>	-1.7	0.014
8	<i>Suv420h1</i>	2.0	0.014
9	<i>Sv2b</i>	69.2	0.005
10	<i>Svil</i>	2.4	0.005
11	<i>Swt1</i>	2.1	0.019
12	<i>Sympk</i>	-1.9	0.033
13	<i>Syn3</i>	-170.5	0.023
14	<i>Syndig1</i>	12.4	0.044
15	<i>Syne3</i>	58.2	0.001
16	<i>Synm</i>	4.3	0.011
17	<i>Syt1</i>	101.3	0.020
18	<i>Syt17</i>	36.4	0.040
19	<i>Syt4</i>	-47.4	0.042
20	<i>Syt6</i>	-100.7	0.028
21	<i>Syt8</i>	189.1	0.019
22	<i>Syvn1</i>	-1.5	0.033
23	<i>Tacc1</i>	1.6	0.014
24	<i>Tacr1</i>	250.9	0.011
25	<i>Tacstd2</i>	475.5	0.007
26	<i>Taf1a</i>	-4.5	0.016
27	<i>Taf9b</i>	-1.9	0.038
28	<i>Tars</i>	-2.2	0.020
29	<i>Tas1r1</i>	-96.2	0.027
30	<i>Tatdn2</i>	1.7	0.029
31	<i>Tbc1d10a</i>	1.7	0.024
32	<i>Tbc1d10b</i>	-1.7	0.026
33	<i>Tbc1d20</i>	-2.5	0.004
34	<i>Tbp</i>	-2.3	0.006
35	<i>Tbx15</i>	-75.4	0.045
36	<i>Tbxa2r</i>	-3.4	0.004
37	<i>Tcf12</i>	-2.3	0.007
38	<i>Tcirg1</i>	2.1	0.015
39	<i>Tcp1</i>	-2.3	0.007
40	<i>Tdh</i>	149.3	0.015
41	<i>Tdp2</i>	2.1	0.007
42	<i>Tefm</i>	-6.9	0.000
43	<i>Tenm2</i>	-36.6	0.049
44	<i>Tep1</i>	2.8	0.004
45	<i>Tesk1</i>	1.8	0.008
46	<i>Tesk2</i>	-6.4	0.030
47	<i>Tf</i>	-5.4	0.010
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<i>Tf</i>	-5.4	0.010
<i>Tfap2e</i>	93.3	0.038
<i>Tfb1m</i>	1.9	0.045
<i>Tgif2</i>	-3.6	0.048
<i>Thbs4</i>	4.4	0.001
<i>Thoc3</i>	-1.6	0.022
<i>Thoc5</i>	-2.1	0.008
<i>Thrap3</i>	-1.8	0.025
<i>Thsd7b</i>	-50.1	0.016
<i>Tiam1</i>	45.1	0.000
<i>Tifa</i>	-7.3	0.000
<i>Timd2</i>	127.6	0.002
<i>Timm13</i>	1.8	0.011
<i>Timm8b</i>	1.6	0.043
<i>Tipr1</i>	-2.1	0.003
<i>Tjp1</i>	1.9	0.045
<i>Tkfc</i>	-2.6	0.028
<i>Tle1</i>	-2.8	0.005
<i>Tle4</i>	-2.2	0.016
<i>Tlr2</i>	-4.3	0.033
<i>Tlr4</i>	248.7	0.000
<i>Tmed2</i>	-1.8	0.002
<i>Tmeff1</i>	-3.0	0.004
<i>Tmem109</i>	1.6	0.010
<i>Tmem135</i>	-2.7	0.042
<i>Tmem170b</i>	365.8	0.003
<i>Tmem178a</i>	-15.2	0.010
<i>Tmem208</i>	1.7	0.017
<i>Tmem259</i>	2.0	0.009
<i>Tmem33</i>	2.0	0.021
<i>Tmem43</i>	-1.8	0.004
<i>Tmem71</i>	-23.7	0.034
<i>Tmem80</i>	2.1	0.039
<i>Tmem86b</i>	-12.1	0.021
<i>Tmem9</i>	-1.9	0.001
<i>Tmod4</i>	22.6	0.032
<i>Tmprss11d</i>	394.4	0.009
<i>Tmprss3</i>	-99.9	0.014
<i>Tmprss6</i>	-94.3	0.029
<i>Tmprss9</i>	12.5	0.040
<i>Tmsb4x</i>	2.0	0.002
<i>Tmtc2</i>	-4.1	0.017
<i>Tmx1</i>	-1.9	0.044
<i>Tnfaip1</i>	-2.3	0.001
<i>Tnfrsf13b</i>	-52.3	0.024
<i>Tnfrsf14</i>	18.2	0.018

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2	<i>Tnfrsf18</i>	-240.7	0.012
3	<i>Tnfrsf19</i>	-3.0	0.001
4	<i>Tnfsf13b</i>	-98.6	0.029
5	<i>Tnmd</i>	-5.4	0.003
6	<i>Tnnb1</i>	-38.0	0.003
7	<i>Tnnb2</i>	964.7	0.002
8	<i>Tnni1</i>	45.5	0.038
9	<i>Tnrc18</i>	2.2	0.015
10	<i>Tnrc6b</i>	2.2	0.006
11	<i>Tns3</i>	1.8	0.030
12	<i>Tob1</i>	2.5	0.014
13	<i>Tom1l1</i>	-3.4	0.008
14	<i>Tox</i>	12.5	0.045
15	<i>Tox4</i>	-2.0	0.002
16	<i>Tp53i13</i>	1.6	0.009
17	<i>Tp53inp2</i>	1.7	0.031
18	<i>Tpm1</i>	-2.2	0.000
19	<i>Tpm4</i>	-2.2	0.001
20	<i>Tpp1</i>	1.8	0.037
21	<i>Tpp1</i>	1.8	0.037
22	<i>Tppp3</i>	3.5	0.018
23	<i>Tpra1</i>	1.6	0.012
24	<i>Tra2b</i>	-1.5	0.010
25	<i>Trappc1</i>	-1.5	0.003
26	<i>Trappc4</i>	1.9	0.002
27	<i>Trex1</i>	2.3	0.002
28	<i>Trib2</i>	2.4	0.002
29	<i>Trim13</i>	-17.1	0.020
30	<i>Trim21</i>	-46.9	0.012
31	<i>Trim37</i>	-2.7	0.038
32	<i>Trim47</i>	2.3	0.002
33	<i>Trim54</i>	187.0	0.013
34	<i>Trim59</i>	-2.1	0.040
35	<i>Trim69</i>	217.0	0.014
36	<i>Trim8</i>	1.5	0.022
37	<i>Trip6</i>	2.0	0.003
38	<i>Trmt10b</i>	2.0	0.030
39	<i>Trmt10c</i>	-1.6	0.036
40	<i>Trpm1</i>	105.4	0.018
41	<i>Trpm8</i>	-100.5	0.019
42	<i>Trpv6</i>	116.7	0.013
43	<i>Trub1</i>	-6.7	0.010
44	<i>Tsacc</i>	99.9	0.018
45	<i>Tspan17</i>	1.9	0.048
46	<i>Tspan6</i>	-1.8	0.002
47	<i>Tspo</i>	2.4	0.001
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2	<i>Tspyl1</i>	-1.5	0.014
3	<i>Ttbk2</i>	4.0	0.027
4	<i>Ttc12</i>	75.4	0.013
5	<i>Ttc17</i>	2.6	0.033
6	<i>Ttf2</i>	2.0	0.031
7	<i>Ttll10</i>	112.0	0.025
8	<i>Ttll3</i>	11.4	0.043
9	<i>Ttyh3</i>	-1.7	0.012
10	<i>Tuba8</i>	199.0	0.000
11	<i>Tubb2a</i>	1.9	0.011
12	<i>Tubb2a</i>	1.9	0.011
13	<i>Tubb4a</i>	222.6	0.014
14	<i>Tubgcp3</i>	2.8	0.006
15	<i>Tusc2</i>	1.6	0.003
16	<i>Txlna</i>	-1.9	0.020
17	<i>Txndc5</i>	-1.5	0.021
18	<i>Tyms</i>	-2.2	0.025
19	<i>Tyrobp</i>	2.3	0.035
20	<i>Uba1</i>	-1.5	0.032
21	<i>Uba2</i>	-3.0	0.020
22	<i>Ubac2</i>	-2.0	0.000
23	<i>Ubash3a</i>	-67.6	0.025
24	<i>Ubc</i>	1.7	0.002
25	<i>Ubd</i>	-72.8	0.047
26	<i>Ube2v2</i>	-1.8	0.003
27	<i>Ubxn2b</i>	-7.3	0.011
28	<i>Ubxn6</i>	1.6	0.004
29	<i>Uchl1</i>	-3.3	0.001
30	<i>Ucp3</i>	494.6	0.008
31	<i>Ugcg</i>	-2.5	0.011
32	<i>Ugdh</i>	-1.8	0.015
33	<i>Uhrf1</i>	-7.7	0.015
34	<i>Umps</i>	-1.8	0.003
35	<i>Unc45a</i>	2.3	0.000
36	<i>Unc5a</i>	770.6	0.007
37	<i>Unc5c</i>	3.7	0.010
38	<i>Unc5d</i>	-35.1	0.046
39	<i>Uqcc1</i>	-1.8	0.039
40	<i>Uqcr11</i>	1.8	0.005
41	<i>Uqcrq</i>	1.6	0.034
42	<i>Urb1</i>	3.3	0.033
43	<i>Use1</i>	2.0	0.003
44	<i>Use1,Ube2z</i>	#N/A	#N/A
45	<i>Usmg5</i>	2.0	0.028
46	<i>Usp11</i>	-3.7	0.000
47	<i>Usp14</i>	-1.5	0.026
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2	<i>Usp19</i>	1.8	0.041
3	<i>Usp24</i>	2.6	0.019
4	<i>Usp33</i>	2.5	0.024
5	<i>Usp36</i>	2.2	0.030
6	<i>Vac14</i>	-2.1	0.009
7	<i>Vamp5</i>	2.2	0.015
8	<i>Vamp8</i>	2.0	0.000
9	<i>Vapb</i>	-2.0	0.006
10	<i>Vil1</i>	-119.4	0.031
11	<i>Vim</i>	1.9	0.005
12	<i>Vipas39</i>	2.2	0.006
13	<i>Vmac</i>	-3.0	0.032
14	<i>Vps13a</i>	4.7	0.008
15	<i>Vps13d</i>	3.3	0.002
16	<i>Vps26a</i>	-2.1	0.021
17	<i>Vps35</i>	-1.7	0.014
18	<i>Vps37b</i>	-2.1	0.013
19	<i>Vps41</i>	-2.4	0.000
20	<i>Vps52</i>	-1.8	0.048
21	<i>Vps53</i>	1.9	0.033
22	<i>Vrk2</i>	-3.5	0.012
23	<i>Vti1a</i>	-4.4	0.001
24	<i>Wars2</i>	-5.0	0.047
25	<i>Wasf2</i>	1.6	0.028
26	<i>Wasl</i>	1.6	0.041
27	<i>Wdfy3</i>	2.8	0.009
28	<i>Wdr5</i>	-1.7	0.035
29	<i>Wdr6</i>	-1.8	0.046
30	<i>Wdr75</i>	-2.9	0.000
31	<i>Wisp2</i>	7.6	0.020
32	<i>Wls</i>	-1.6	0.034
33	<i>Wnt11</i>	-3.2	0.009
34	<i>Wnt5b</i>	2.6	0.004
35	<i>Wrap73</i>	1.7	0.042
36	<i>Xk</i>	-35.6	0.018
37	<i>Xkr4</i>	33.9	0.034
38	<i>Xkr6</i>	32.9	0.034
39	<i>Xpo1</i>	-2.2	0.025
40	<i>Xpo6</i>	-2.2	0.008
41	<i>Xpot</i>	-2.2	0.012
42	<i>Xrcc1</i>	1.8	0.002
43	<i>Xrcc5</i>	-2.6	0.001
44	<i>Yaf2</i>	-1.6	0.015
45	<i>Ykt6</i>	-2.6	0.006
46	<i>Ylpm1</i>	1.8	0.045
47	<i>Ythdc1</i>	2.0	0.025
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2	<i>Ywhab</i>	-1.5	0.002
3	<i>Ywhae</i>	-1.7	0.000
4	<i>Ywhag</i>	1.7	0.014
5	<i>Ywhaz</i>	-1.7	0.004
6	<i>Zbed3</i>	-1.7	0.036
7	<i>Zbp1</i>	-40.1	0.026
8	<i>Zbp1</i>	-40.1	0.026
9	<i>Zbtb16</i>	337.2	0.001
10	<i>Zbtb7c</i>	3.5	0.018
11	<i>Zc3h10</i>	2.6	0.002
12	<i>Zc3h14</i>	-1.9	0.010
13	<i>Zcchc12</i>	-3.4	0.008
14	<i>Zcrb1</i>	1.5	0.025
15	<i>Zdhhc20</i>	-2.4	0.001
16	<i>Zdhhc6</i>	-1.9	0.012
17	<i>Zfp2</i>	247.2	0.005
18	<i>Zfp263</i>	-2.3	0.019
19	<i>Zfp280b</i>	9.6	0.029
20	<i>Zfp394</i>	2.1	0.045
21	<i>Zfp410</i>	-1.7	0.030
22	<i>Zfp422</i>	-1.9	0.003
23	<i>Zfp467</i>	2.3	0.031
24	<i>Zfp483</i>	-181.1	0.023
25	<i>Zfp513</i>	1.8	0.041
26	<i>Zfp521</i>	-2.2	0.018
27	<i>Zfp641</i>	27.7	0.033
28	<i>Zfp68</i>	-2.0	0.012
29	<i>Zgpat</i>	2.4	0.027
30	<i>Zim1</i>	-290.1	0.014
31	<i>Zmpste24</i>	-5.5	0.000
32	<i>Znhit1</i>	1.9	0.012
33	<i>Znrd1</i>	1.7	0.037
34	<i>Zpbp</i>	-114.6	0.006
35	<i>Zswim5</i>	184.5	0.008
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Appendix Table 2

The original proteomic analysis data of stretched PDL cells showed in Figure 4.

Accession	Gene	LFQ intensity Control	LFQ intensity Stretched
A0A024R442	DNPEP	0	20.9996891
A0A075B785	RELCH	0	19.76844597
A0A087WTA8	COL1A2	25.22523308	26.31858635
A0A087WVZ9	POLR2E	0	20.16643715
A0A087WX58	HDGFL2	0	19.65448952
A0A087WXC5	NDUFA10	22.09055138	0
A0A087WYV8	FBN2	19.73524284	20.74386215
A0A0A0MRE1	EXOC7	0	20.59914207
A0A0A0MSK4	GPSM1	21.75103188	20.19568443
A0A0A0MTN9	FDXR	0	20.98454094
A0A0A0MTR7	RNF213	23.30827522	24.40379715
A0A0A6YYA0	TMED7-TICAM2	21.09119797	22.54521751
A0A0B4J2A0	None	0	19.78540421
A0A0C4DFM1	TM9SF4	21.73148537	20.58682823
A0A0C4DG40	SYNE1	23.24419022	24.31257439
A0A0G2JNZ5	GBA	0	22.26023293
A0A0U1RR22	PACSIN2	0	22.15375519
A0A1B0GTU1	ZC3H11B	0	17.82059097
A0A1B0GWF2	STXBP1	20.82973862	22.27295685
A0A1W2PR68	ME2	0	19.77781677
A0A2R8Y430	GSS	0	22.14416885
A0A2R8YF43	CSNK2A1	22.16628456	21.01202202
A0A3B3IS01	DARS2	19.57568359	0
B1ALD9	POSTN	21.65460205	20.32410622
B1ANM7	FAF1	21.37023354	20.30463219
B4E1E4	EIF4E2	0	19.40582275
B8ZZC5	GLS	20.10686874	0
C9JBI3	PSPH	0	18.98061371
C9JJ54	WDFY1	19.68905258	0
E7EWK3	DHX36	0	20.04686737
E9PB90	HK2	22.67480278	21.65110207
E9PF19	TBL2	21.46188927	20.36474228
E9PGM1	EIF4G1	26.33698273	24.98767471
E9PHV5	ITPRID2	19.72468948	20.93531418
E9PKU7	GANAB	0	20.05959702
E9PLK3	NPEPPS	24.54639626	25.80466843
E9PNU4	STX5	0	20.20741081
E9PQP3	ARFGAP2	0	19.8045311
F2Z2X4	XPO4	0	19.36851883
F5H4B6	ALDH16A1	20.39947319	0

<b>F5H5N1</b>	<b>NDUFS7</b>	0	20.1316967
<b>F8VSC5</b>	<b>SCYL2</b>	0	20.32432556
<b>F8W020</b>	<b>NAP1L1</b>	23.19088554	24.30340576
<b>F8W1F5</b>	<b>FMNL3</b>	0	19.6111908
<b>F8W808</b>	<b>NAA10</b>	21.89081955	20.4582386
<b>F8W9T3</b>	<b>SNX4</b>	0	21.89969635
<b>G3V126</b>	<b>ATP6V1H</b>	0	18.98281479
<b>G3V529</b>	<b>DDX24</b>	0	18.44596863
<b>G5E9S8</b>	<b>KLC1</b>	23.14177132	24.31741333
<b>H0YDP7</b>	<b>MRPL49</b>	0	20.50581551
<b>J3KTF8</b>	<b>ARHGDIA</b>	24.56307983	25.60501099
<b>J3QLR8</b>	<b>MRPS23</b>	0	19.49917221
<b>J3QR09</b>	<b>RPL19</b>	22.55912781	23.77283669
<b>M0R026</b>	<b>ILVBL</b>	21.18252945	19.68642235
<b>M0R208</b>	<b>CLPP</b>	20.40789795	22.10980606
<b>O00267</b>	<b>SUPT5H</b>	0	20.00237083
<b>O00754</b>	<b>MAN2B1</b>	0	20.7157383
<b>O14818</b>	<b>PSMA7</b>	24.01154327	25.14390373
<b>O15173</b>	<b>PGRMC2</b>	22.74915123	23.92315865
<b>O15270</b>	<b>SPTLC2</b>	0	19.53425407
<b>O15427</b>	<b>SLC16A3</b>	23.23410606	22.17292023
<b>O15460</b>	<b>P4HA2</b>	24.34638023	26.01073265
<b>O43390</b>	<b>HNRNPR</b>	21.59418488	23.08321571
<b>O60502</b>	<b>OGA</b>	0	21.01352119
<b>O60762</b>	<b>DPM1</b>	19.60188293	20.8239994
<b>O75534</b>	<b>CSDE1</b>	21.91338539	22.95976639
<b>O75643</b>	<b>SNRNP200</b>	26.44395256	25.00906754
<b>O75844</b>	<b>ZMPSTE24</b>	21.97571754	20.68953133
<b>O75962</b>	<b>TRIO</b>	20.65394783	21.80644417
<b>O75976</b>	<b>CPD</b>	0	21.04092979
<b>O94804</b>	<b>STK10</b>	0	17.59433937
<b>O95197</b>	<b>RTN3</b>	22.27332687	20.819561
<b>O95248</b>	<b>SBF1</b>	0	21.51123238
<b>O95810</b>	<b>CAVIN2</b>	0	19.57767677
<b>O95881</b>	<b>TXNDC12</b>	0	20.94177628
<b>O96005</b>	<b>CLPTM1</b>	22.37983513	21.17718506
<b>P02452</b>	<b>COL1A1</b>	26.02312088	28.7821312
<b>P02461</b>	<b>COL3A1</b>	21.85866928	23.9216156
<b>P02545</b>	<b>LMNA</b>	28.88495064	29.89865112
<b>P02792</b>	<b>FTL</b>	23.62644958	22.54158401
<b>P04080</b>	<b>CSTB</b>	23.54957199	22.35901451
<b>P04632</b>	<b>CAPNS1</b>	24.03204155	25.27476311
<b>P04792</b>	<b>HSPB1</b>	26.62714577	27.82420158
<b>P04818</b>	<b>TYMS</b>	21.41142082	20.24898911
<b>P05997</b>	<b>COL5A2</b>	19.73646545	21.18924332
<b>P07814</b>	<b>EPRS</b>	24.96146393	26.25281143
<b>P08243</b>	<b>ASNS</b>	22.13842964	23.32909775

P08574	CYC1	0	20.90873909
P08648	ITGA5	25.22574806	24.18737221
P09960	LTA4H	21.50149727	22.81188202
P0DMV9	HSPA1B	29.0905323	27.32551575
P12081	HARS	24.30528641	25.34235001
P14923	JUP	20.95695114	0
P15104	GLUL	0	20.75287056
P16234	PDGFRA	0	20.9249897
P16930	FAH	21.85178566	20.74779892
P17066	HSPA6	28.77596092	27.75748062
P19174	PLCG1	0	19.5958519
P19474	TRIM21	0	19.35287476
P20908	COL5A1	21.16090965	22.27810097
P21964	COMT	22.38226509	23.46811867
P23381	WARS	23.40743256	24.44335365
P24928	POLR2A	20.53763199	19.08085442
P26022	PTX3	0	19.87612724
P26038	MSN	28.74890327	29.82072258
P26373	RPL13	25.4160614	26.60385323
P27348	YWHAQ	26.22118187	27.4228611
P28288	ABCD3	21.29283142	19.83644104
P30038	ALDH4A1	0	18.69149208
P30405	PPIF	23.03175545	22.02116776
P31153	MAT2A	23.43478966	22.30924797
P32119	PRDX2	25.56575584	24.35137749
P32455	GBP1	20.91342163	22.04620171
P35354	PTGS2	22.50054932	20.74246407
P35573	AGL	0	18.90124321
P42167	TMPO	20.45352364	21.76198578
P43487	RANBP1	22.69242859	23.94628143
P46821	MAP1B	27.4512043	26.03632545
P46937	YAP1	21.46173859	22.57327652
P46940	IQGAP1	27.27382088	28.48834229
P47914	RPL29	23.20067596	24.29459953
P49748	ACADVL	25.07842827	26.20894051
P50395	GDI2	26.025383	27.03128433
P50416	CPT1A	23.39610672	22.20943451
P51809	VAMP7	0	19.97687149
P51970	NDUFA8	21.54297638	19.81770515
P52630	STAT2	20.81151009	21.92524338
P55084	HADHB	25.01979446	23.79213333
P56545	CTBP2	21.70956612	22.81381989
P57764	GSDMD	0	19.04390907
P61586	RHOA	0	22.79070282
P61619	SEC61A1	24.79808044	23.63533401
P62826	RAN	25.3025341	26.37102509
P67809	YBX1	25.56435966	24.45349884

P78559	MAP1A	23.87107658	24.99183273
Q00688	FKBP3	21.51638603	23.73106956
Q04917	YWHAH	24.16622353	25.20988846
Q06124	PTPN11	21.06716919	22.37581062
Q06203	PPAT	0	20.50057411
Q08378	GOLGA3	21.67620277	22.77782059
Q12965	MYO1E	20.13746071	21.31959343
Q13131	PRKAA1	0	21.00422287
Q13242	SRSF9	19.10469627	20.44909668
Q13596	SNX1	21.8387661	23.32991982
Q14152	EIF3A	24.92718887	26.21811676
Q14696	MESD	19.84509277	21.00374222
Q14789	GOLGB1	24.66871452	23.57080078
Q15021	NCAPD2	0	20.3668766
Q15056	EIF4H	23.36826324	24.77660751
Q15075	EEA1	23.31741333	24.69104385
Q15233	NONO	24.7138195	25.76789665
Q16134	ETFDH	21.16029549	0
Q16513	PKN2	19.69333076	20.82150841
Q16658	FSCN1	25.69144249	26.86714554
Q16778	HIST2H2BE	26.90644264	25.62419128
Q16822	PCK2	22.51982117	24.02647972
Q16878	CDO1	0	23.31451225
Q5JRG1	NUP58	0	20.33123207
Q5T0I0	GSN	21.1754818	22.3467598
Q5VYK3	ECPAS	22.48892975	24.10093307
Q68CQ7	GLT8D1	0	21.56592941
Q68E01	INTS3	0	19.13560867
Q6P2E9	EDC4	19.89511681	21.12760925
Q7Z3U7	MON2	0	21.72558975
Q8IVF2	AHNAK2	21.0956459	0
Q8IWJ2	GCC2	20.04126358	21.07463455
Q8N129	CNPY4	19.50589371	0
Q8TBA6	GOLGA5	19.2819519	0
Q8TCT9	HM13	25.04963684	24.03355408
Q8TDD1	DDX54	0	19.40621758
Q8TEX9	IPO4	21.96370506	23.04977798
Q8WU90	ZC3H15	20.30273628	21.33576393
Q92575	UBXN4	0	20.73073959
Q92629	SGCD	0	19.04788017
Q92734	TFG	23.73055267	24.79872322
Q92882	OSTF1	20.70497513	21.89145088
Q96CG8	CTHRC1	21.28263092	22.5556221
Q96CT7	CCDC124	0	19.65881729
Q96JQ0	DCHS1	18.9074192	0
Q96SB3	PPP1R9B	21.21299934	0
Q96TA1	FAM129B	26.7624321	24.93035126

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Q99715	COL12A1	25.5644474	27.04228592
Q99747	NAPG	0	20.63962364
Q99805	TM9SF2	21.15961838	20.02431679
Q99832	CCT7	25.16970634	26.43934822
Q9BPW8	NIPSNAP1	0	20.66440201
Q9BQ67	GRWD1	0	19.73229599
Q9BQS8	FYCO1	20.9930687	22.06111526
Q9BRF8	CPPED1	0	21.15165138
Q9BW60	ELOVL1	22.21208	21.1392746
Q9BY44	EIF2A	22.04266739	20.94713783
Q9H1B7	IRF2BPL	0	18.87306595
Q9H223	EHD4	0	20.26956558
Q9H2U2	PPA2	0	21.18507385
Q9HAV7	GRPEL1	20.83259964	22.38094521
Q9HB40	SCPEP1	0	20.93675232
Q9HCL0	PCDH18	0	19.58913612
Q9HD45	TM9SF3	22.06999016	20.69251251
Q9NRY4	ARHGAP35	0	19.44497871
Q9NSD9	FARSB	22.56020164	24.20329285
Q9NUQ8	ABCF3	0	19.8791523
Q9NV70	EXOC1	19.37553596	0
Q9NVI7	ATAD3A	22.91378593	24.31319809
Q9NW15	ANO10	0	20.39089584
Q9NX08	COMMD8	0	20.09493828
Q9NXG2	THUMPD1	0	21.14413834
Q9NZB2	FAM120A	25.2062397	23.61717224
Q9NZN4	EHD2	25.39447212	26.43766594
Q9P2R3	ANKFY1	21.45848846	22.65425301
Q9UBG0	MRC2	23.40781975	24.75302315
Q9UH99	SUN2	19.84743309	21.2696228
Q9UL25	RAB21	21.68863487	22.91340256
Q9ULT8	HECTD1	0	20.53107643
Q9UMX0	UBQLN1	0	21.44955063
Q9UN70	PCDHGC3	0	20.26647949
Q9UNW1	MINPP1	0	20.22163963
Q9UQE7	SMC3	22.4522171	21.36420822
Q9Y224	RTRAF	22.34708405	23.44113731
Q9Y230	RUVBL2	23.94529915	24.95464706
Q9Y281	CFL2	0	21.72425652
Q9Y2X3	NOP58	0	21.9932766
Q9Y3I0	RTCB	23.71187782	24.85562134
Q9Y512	SAMM50	0	21.21240616
Q9Y5S2	CDC42BPB	19.38237	20.63794518
Q9Y5S9	RBM8A	21.61867332	20.58389473
Q9Y608	LRRFIP2	0	20.42070007
R4GNG3	GIT2	0	19.97084808
S4R3Z2	AKR1C3	21.77671814	0

**Appendix Table 3**

The antibodies, primers and protein used in the study.

<b>Primary antibodies (Immunofluorescence)</b>					
<b>Antigen</b>	<b>Figure</b>	<b>Diluting factor</b>	<b>Company</b>	<b>Cat. No.</b>	<b>Batch No.</b>
Notch 1 ICD	2D	1:200	e-Bioscience	14-5785-82	E04375-261
Total Notch1	2E	1:200	Cell Signalling	4380s	lot 2
Dll1	2F	1:200	R&D Systems	AF5026	
Osteopontin	2G	1:100	Dr Larry fisher (NIH)	LF-166 hOPN (C-terminus)	
Periostin	1C, 3H-J, App. 2A	1:400	Abcam	AB14041	
Notch 2 ICD	2E	1:200	Sigma	SAB4502022	410353
Lamin A/C	5B	1:200	Cell signalling	4777s	Lot 1
Lamin A/C	5E	1:200	Santa Cruz	sc-20681	A1116

<b>Secondary antibodies (Immunofluorescence)</b>				
<b>Target</b>	<b>Dilution</b>	<b>Company</b>	<b>Cat. No.</b>	<b>Lot</b>
Alexa 568 Donkey anti-Mouse IgG	1:500	Life Technologies	A10037	1303018
Alexa 568 Donkey anti-Rabbit IgG	1:500	Life Technologies	A10042	1964370
Alexa 568 Donkey anti-Rabbit IgG	1:500	Abcam	Ab175470	
Alexa 488 Donkey anti-Sheep IgG	1:300	Life Technologies	A11015	1322311
Alexa 488 Donkey anti-Mouse IgG	1:300	Life Technologies	A21202	1796361

<b>Antibodies (Western Blotting)</b>					
<b>Antigen</b>	<b>Figure</b>	<b>Diluting factor</b>	<b>Company</b>	<b>Cat. No.</b>	<b>Batch No.</b>
GapDH	5	1:500	Santa Cruz	SC-32233	H2114
Lamin A/C	5	1:400	Cell Signalling	4777	
Anti-Rabbit HRP	5	1:500	Cell Signalling	7074P2	
Anti-Mouse HRP	5	1:500	Cell Signalling	7076P2	

<b>Primers</b>			
<b>Gene (mouse)</b>	<b>Forward primer (5'-3')</b>	<b>Reverse primer (5'-3')</b>	<b>PCR Product size</b>

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Hes1	TGAGCCAGCTGAAAACACTG	AGCACACTTGGGTCTGTGC	160
DLL1	GCACGGACCTCAAGTACTCC	ATGCTGCTCATCACATCCAG	200
Hey1	CTTTTGGTGCATGGAAGTGT	CAGTTCAGTGGAGGTCGTTT	152
DLL4	GCGAGAAGAAAGTGGACAGG	ATTCTCCAGGTCATGGCAAG	185
Jag1	ATCGTGCTGCCTTTCAGTTT	ATTGCAGCCAAAGCCATAGT	234
Acta2	CAGATGTGGATCAGCAAACA	TGGCTAGGAATGATTTGGAA	161
BGLAP	CAGCGAGGTAGTGAAGAG	GGGAAGAGGAAAGAAGGG	249
Runx2	CTCTGACCGCCTCAGTGATT	GGCTCAGGTAGGAGGGGTAA	200
Periostin	CAAAACTGAAGGACCCACAC	TATTTCCACAGGCACTCCAT	154
Sparc	GTGCAGAGGAAACCGAAGAG	AAGTGGCAGGAAGAGTCGAA	200
GapDH	ATCACTGCCACCCAGAAGAC	CAGTGAGCTTCCCGTTCAG	148
36B4	GCAATGTTGCCAGTGTCTGT	GCCTTGACCTTTTCAGCAAG	142
SPP1	TTGCAGTGATTTGCTTTTGC	GTCATGGCTTTCGTTGGACT	200
Dlk1	GGCTTCATCGACAAGACCTG	CAGGTCTCGCACTTGTTGAG	185

Recombinant Proteins			
Protein	Company	Cat. No.	Lot
Human Jagged 1	R&D	1277-JG-050	RZL1713041